

PATENT APPLICATION

T2R, A NOVEL FAMILY OF TASTE RECEPTORS

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CROSS-REFERENCES TO RELATED APPLICATIONS

This application claims priority to and is a continuation-in-part of USSN 09/393,634, filed September 10, 1999, which is herein incorporated by reference in its entirety.

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STATEMENT AS TO FEDERALLY SPONSORED RESEARCH AND DEVELOPMENT

This invention was made with government support under Grant No. 5R01 DC03160, awarded by the National Institutes of Health. The government has certain rights in this invention.

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FIELD OF THE INVENTION

The invention provides isolated nucleic acid and amino acid sequences of taste cell specific G-protein coupled receptors, antibodies to such receptors, methods of detecting such nucleic acids and receptors, and methods of screening for modulators of taste cell specific G-protein coupled receptors.

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BACKGROUND OF THE INVENTION

Taste transduction is one of the most sophisticated forms of chemotransduction in animals (*see, e.g.*, Margolskee, *BioEssays* 15:645-650 (1993); Avenet & Lindemann, *J. Membrane Biol.* 112:1-8 (1989)). Gustatory signaling is found throughout the animal kingdom, from simple metazoans to the most complex of vertebrates; its main purpose is to provide a reliable signaling response to non-volatile ligands. Each of these modalities is thought to be mediated by distinct signaling pathways mediated by receptors or channels, leading to receptor cell depolarization, generation of a receptor or action potential, and release of neurotransmitter at gustatory afferent neuron synapses (*see, e.g.*, Roper, *Ann. Rev. Neurosci.* 12:329-353 (1989)).

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Mammals are believed to have five basic taste modalities: sweet, bitter, sour, salty, and umami (the taste of monosodium glutamate) (see, e.g., Kawamura & Kare, *Introduction to Umami: A Basic Taste* (1987); Kinnamon & Cummings, *Ann. Rev. Physiol.* 54:715-731(1992); Lindemann, *Physiol. Rev.* 76:718-766 (1996); Stewart *et al.*, *Am. J. Physiol.* 272:1-26 (1997)). Extensive psychophysical studies in humans have reported that different regions of the tongue display different gustatory preferences (see, e.g., Hoffmann, *Menchen. Arch. Path. Anat. Physiol.* 62:516-530 (1875); Bradley *et al.*, *Anatomical Record* 212: 246-249 (1985); Miller & Reedy, *Physiol. Behav.* 47:1213-1219 (1990)). Also, numerous physiological studies in animals have shown that taste receptor cells may selectively respond to different tastants (see, e.g., Akabas *et al.*, *Science* 242:1047-1050 (1988); Gilbertson *et al.*, *J. Gen. Physiol.* 100:803-24 (1992); Bernhardt *et al.*, *J. Physiol.* 490:325-336 (1996); Cummings *et al.*, *J. Neurophysiol.* 75:1256-1263 (1996)).

In mammals, taste receptor cells are assembled into taste buds that are distributed into different papillae in the tongue epithelium. Circumvallate papillae, found at the very back of the tongue, contain hundreds (mice) to thousands (human) of taste buds and are particularly sensitive to bitter substances. Foliate papillae, localized to the posterior lateral edge of the tongue, contain dozens to hundreds of taste buds and are particularly sensitive to sour and bitter substances. Fungiform papillae containing a single or a few taste buds are at the front of the tongue and are thought to mediate much of the sweet taste modality.

Each taste bud, depending on the species, contains 50-150 cells, including precursor cells, support cells, and taste receptor cells (see, e.g., Lindemann, *Physiol. Rev.* 76:718-766 (1996)). Receptor cells are innervated at their base by afferent nerve endings that transmit information to the taste centers of the cortex through synapses in the brain stem and thalamus. Elucidating the mechanisms of taste cell signaling and information processing is critical for understanding the function, regulation, and “perception” of the sense of taste.

Although much is known about the psychophysics and physiology of taste cell function, very little is known about the molecules and pathways that mediate these sensory signaling responses (reviewed by Gilbertson, *Current Opin. Neurobiol.* 3:532-539 (1993)). Electrophysiological studies suggest that sour and salty tastants modulate taste cell function by direct entry of H^+ and Na^+ ions through specialized membrane channels on the apical surface of the cell. In the case of sour compounds, taste cell

depolarization is hypothesized to result from H⁺ blockage of K⁺ channels (*see, e.g.,* Kinnamon *et al.*, *Proc. Nat'l Acad. Sci. USA* 85: 7023-7027 (1988)) or activation of pH-sensitive channels (*see, e.g.,* Gilbertson *et al.*, *J. Gen. Physiol.* 100:803-24 (1992)); salt transduction may be partly mediated by the entry of Na⁺ via amiloride-sensitive Na⁺ channels (*see, e.g.,* Heck *et al.*, *Science* 223:403-405 (1984); Brand *et al.*, *Brain Res.* 207-214 (1985); Avenet *et al.*, *Nature* 331: 351-354 (1988)).

Sweet, bitter, and umami transduction are believed to be mediated by G-protein-coupled receptor (GPCR) signaling pathways (*see, e.g.,* Striem *et al.*, *Biochem. J.* 260:121-126 (1989); Chaudhari *et al.*, *J. Neuros.* 16:3817-3826 (1996); Wong *et al.*, *Nature* 381: 796-800 (1996)). Confusingly, there are almost as many models of signaling pathways for sweet and bitter transduction as there are effector enzymes for GPCR cascades (*e.g.,* G protein subunits, cGMP phosphodiesterase, phospholipase C, adenylate cyclase; *see, e.g.,* Kinnamon & Margolskee, *Curr. Opin. Neurobiol.* 6:506-513 (1996)). However, little is known about the specific membrane receptors involved in taste transduction, or many of the individual intracellular signaling molecules activated by the individual taste transduction pathways. Identification of such molecules is important given the numerous pharmacological and food industry applications for bitter antagonists, sweet agonists, and other modulators of taste.

One taste-cell specific G protein that has been identified is called Gustducin (McLaughlin *et al.*, *Nature* 357:563-569 (1992)). This protein is proposed to be involved in the detection of certain bitter and sweet tastes since gustducin knockout mice show decreased sensitivity to some sweet and bitter tastants (Wong *et al.*, *Nature* 381:796-800 (1996)), and because gustducin is expressed in a significant subset of cells from all types of taste papillae (McLaughlin *et al.*, *Nature* 357:563-569 (1992)). In addition, gustducin can be activated *in vitro* by stimulating taste membranes with bitter compounds, likely through the activation of bitter receptors (Ming *et al.*, *PNAS* 95:8933-8938 (1998)).

Recently, two novel GPCRs were identified and found to be specifically expressed in taste cells. While these receptor proteins, called TR1 and TR2, appear to be directly involved in taste reception (Hoon *et al.*, *Cell* 96:541-551 (1999)), they are only expressed in a fraction of mammalian taste receptor cells. For example, neither of the genes are extensively expressed in Gustducin-expressing cells. Thus, it is clear that additional taste-involved GPCRs remain to be discovered.

Genetic studies in mammals have identified numerous loci that are involved in the detection of taste. For example, psychophysical tasting studies have shown that humans can be categorized as tasters, non-tasters, and super-tasters for the bitter substance PROP (6-n-propylthiouracil), and that PROP tasting may be conferred by a dominant allele, with non-tasters having two recessive alleles and tasters having at least one dominant allele (see Bartoshuk *et al.*, *Physiol Behav* 56(6):1165-71; 58:203-204 (1994)). Recently, a locus involved in PROP tasting has been mapped to human interval 5p15 (Reed *et al.*, *Am. J. Hum. Genet.*, 64(5):1478-80 (1999)). The PROP tasting gene present at the 5p15 locus has yet to be described, however.

In addition, a number of genes involved in taste have been mapped in mice. For example, a cluster of genes involved in bitter-taste detection has been mapped to a region of chromosome 6 in mice (Lush *et al.*, *Genet Res.* 66:167-174 (1995)).

The identification and isolation of novel taste receptors and taste signaling molecules would allow for new methods of pharmacological and genetic modulation of taste transduction pathways. For example, the availability of receptor and channel molecules would permit the screening for high affinity agonists, antagonists, inverse agonists, and modulators of taste cell activity. Such taste modulating compounds would be useful in the pharmaceutical and food industries to customize taste. In addition, such taste cell specific molecules can serve as invaluable tools in the generation of taste topographic maps that elucidate the relationship between the taste cells of the tongue and taste sensory neurons leading to taste centers in the brain.

SUMMARY OF THE INVENTION

The present invention thus provides novel nucleic acids encoding a family of taste-cell specific G-protein coupled receptors. These nucleic acids and the polypeptides that they encode are referred to as the "T2R" family of G-protein coupled taste receptors. These receptors are also referred to as the "SF" family of G-protein coupled taste receptors. This novel family of GPCRs includes components of the taste transduction pathway. In particular, members of this family are involved in the detection of bitter tastes.

In one aspect, the present invention provides a method for identifying a compound that modulates taste signaling in taste cells, the method comprising the steps of: (i) contacting a taste transduction G-protein coupled receptor polypeptide with the compound, the polypeptide comprising at least about 50% amino acid identity to a

sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171; and (ii) determining the functional effect of the compound upon the polypeptide.

In another aspect, the present invention provides a method for identifying a compound that modulates taste signaling in taste cells, the method comprising the steps of: (i) contacting a taste transduction G-protein coupled receptor polypeptide with the compound, the polypeptide comprising greater than about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164; and (ii) determining the functional effect of the compound upon the polypeptide.

In another aspect, the present invention provides a method for identifying a compound that modulates taste signaling in taste cells, the method comprising the steps of: (i) contacting a polypeptide comprising an extracellular domain or transmembrane region, or combination thereof, of a taste transduction G-protein coupled receptor with the compound, the extracellular domain or transmembrane region comprising greater than about 60% amino acid sequence identity to the extracellular domain or transmembrane

region of a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164; and (ii) determining the functional effect of the compound upon the extracellular domain or transmembrane region.

In one embodiment, the polypeptide has G-protein coupled receptor activity. In another embodiment, the functional effect is a chemical effect. In another embodiment, the functional effect is a physical effect. In another embodiment, the functional effect is determined by measuring binding of the compound to an extracellular domain of the polypeptide. In another embodiment, the functional effect is determined by measuring radiolabeled GTP binding to the polypeptide. In another embodiment, the polypeptide is recombinant. In another embodiment, the polypeptide comprises an extracellular domain or transmembrane region or a combination of an extracellular domain and transmembrane region that is covalently linked to a heterologous polypeptide, forming a chimeric polypeptide. In another embodiment, the polypeptide is linked to a solid phase, either covalently or non-covalently. In another embodiment, the polypeptide is from a rat, a mouse, or a human.

In another embodiment, the polypeptide is expressed in a cell or a cell membrane. In another embodiment, the cell is a eukaryotic cell. In another embodiment, the functional effect is measured by determining changes in the electrical activity of a cell expressing the polypeptide. In another embodiment, the functional effect of the compound upon the polypeptide is determined by measuring changes in intracellular cAMP, cGMP, IP3, or Ca^{2+} in a cell expressing the polypeptide. In another embodiment, a change in intracellular Ca^{2+} in the cell is detected by detecting FURA-2 dependent fluorescence in the cell. In another embodiment, the cell is a eukaryotic cell. In another embodiment, the cell is an HEK-293 cell. In another embodiment, the polypeptide is a fusion protein comprising at least about 20 consecutive N-terminal amino acids of a rhodopsin protein. In another embodiment, the rhodopsin protein is a bovine rhodopsin. In another embodiment, the cell comprises G α 15. In another embodiment, the polypeptide is expressed in a cell, and the polypeptide is contacted with the compound in the presence of a bitter tastant, wherein a difference in the functional effect of the bitter tastant on the cell in the presence of the compound and the functional effect of the bitter tastant on the cell in the absence of the compound indicates that the compound is capable of modulating taste signaling in taste cells.

In another embodiment, the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID

NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

In another aspect, the present invention provides an isolated nucleic acid encoding a taste transduction G-protein coupled receptor, the receptor comprising greater than about 50% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

In another aspect, the present invention provides an isolated nucleic acid encoding a taste transduction G-protein coupled receptor, wherein the nucleic acid is amplified by primers that selectively hybridize to the same sequence as degenerate primer sets encoding amino acid sequences selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

In another aspect, the present invention provides an isolated nucleic acid encoding a taste transduction G-protein coupled receptor, the receptor comprising greater than about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

In another aspect, the present invention provides an isolated nucleic acid encoding a taste transduction G-protein coupled receptor, wherein the nucleic acid specifically hybridizes under highly stringent conditions to a nucleic acid having a nucleotide sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID

NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165 but not to a nucleic acid having a
5 nucleotide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID
10 NO:54, SEQ ID NO:57, SEQ ID NO:61, and SEQ ID NO:63.

In another aspect, the present invention provides an isolated nucleic acid encoding an extracellular domain or transmembrane region or a combination thereof of a taste transduction G-protein coupled receptor, the extracellular domain or transmembrane region having greater than about 60% amino acid sequence identity to the extracellular
15 domain or transmembrane region of a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID
20 NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ
25 ID NO:164.

In one embodiment, the nucleic acid encodes a receptor that specifically binds to polyclonal antibodies generated against a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID
30 NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID

NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164, but not to polyclonal antibodies generated against a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, and SEQ ID NO:76.

In another embodiment, the nucleic acid encodes a receptor comprising an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

In another embodiment, the nucleic acid comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, ~~SEQ ID NO:120~~, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID

NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165.

5 In another embodiment, the nucleic acid encodes a receptor that has G-protein coupled receptor activity. In another embodiment, the nucleic acid is from a rat or a mouse.

In another embodiment, the nucleic acid encodes an extracellular domain or transmembrane region or combination thereof linked to a heterologous polypeptide, forming a chimeric polypeptide. In another embodiment, the nucleic acid encodes the
10 extracellular domain of a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID
15 NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, SEQ ID NO:164, SEQ ID
20 NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

In another aspect, the present invention provides an expression vector comprising any of the above nucleic acids. In another aspect, the present invention provides isolated cells comprising the expression vector.

25 In another aspect, the present invention provides an isolated taste transduction G-protein coupled receptor, the receptor comprising greater than about 50% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

30 In another aspect, the present invention provides an isolated taste transduction G-protein coupled receptor, the receptor comprising greater than about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID

NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

In one embodiment, the receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171.

In another embodiment, the receptor specifically binds to polyclonal antibodies generated against a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164, but not to polyclonal antibodies generated against a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ

ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, and SEQ ID NO:76. In another embodiment, the receptor has G-protein coupled receptor activity. In another embodiment, the receptor is from a rat or a mouse.

10 In another aspect, the present invention provides an isolated polypeptide comprising an extracellular domain or a transmembrane region or a combination thereof of a taste transduction G-protein coupled receptor, the extracellular domain or transmembrane region comprising greater than about 60% amino acid sequence identity to the extracellular domain or transmembrane region of a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

25 In one embodiment, the polypeptide encodes the extracellular domain or transmembrane region of a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID

NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171. In another embodiment, the extracellular domain or transmembrane region is covalently linked to a heterologous polypeptide, forming a chimeric polypeptide.

5 In one aspect, the present invention provides an antibody that selectively binds to the receptor comprising greater than about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

 In another aspect, the present invention provides an expression vector comprising a nucleic acid encoding a taste transduction G-protein coupled receptor, wherein the receptor is expressed in a taste cell, the receptor comprising greater than
20 about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164.

30 In another aspect, the present invention provides a host cell transfected with the expression vector.

 In another aspect, the present invention provides an expression cassette comprising a polynucleotide sequence that encodes a human taste transduction G protein coupled receptor, operably linked to a heterologous promoter, wherein the receptor

comprises an amino acid sequence comprising greater than about 60% amino acid sequence identity to a sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, and SEQ ID NO:76.

In one embodiment, the receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, and SEQ ID NO:76.

In another aspect, the present invention provides an isolated eukaryotic cell comprising the expression cassette.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 demonstrates that G α 15 couples the activation of μ opioid receptor and mGluR1 receptor to the release of intracellular calcium. HEK-293 cells were transiently transfected with the G α i coupled μ opioid receptor or the G α q coupled mGluR1 receptor. Transfected cells containing G α 15 were assayed for increases in [Ca²⁺]_i before (a, b) and after (c, d) the addition of receptor agonists: (c) 10 μ M DAMGO

and (d) 20 μ M trans (\pm) 1-amino-1,3 cyclopentane dicarboxylic acid, (ACPD). Ligand- and receptor-dependent increase in $[Ca^{2+}]_i$ were dependent on $G\alpha 15$ (panels e, f). Scales indicate $[Ca^{2+}]_i$ (nM) determined from FURA-2 emission ratios.

Figure 2 shows that the first 39 amino acids of bovine rhodopsin effectively targets T2Rs to the plasma membrane of HEK-293 cells.

Immunofluorescence staining of non-permeabilized cells transfected with representative rho-T2R fusions was detected using an anti-rhodopsin mAb B6-30.

Figure 3 demonstrates that T2R receptors are stimulated by bitter compounds. HEK-293 cells were transfected with rho-mT2R5 (a, d, g), rho-hT2R4 (b, e, h), and rho-mT2R8 (c, f, i). Cells expressing mT2R5 were stimulated using 1.5 μ M cycloheximide (d, g) and those expressing hT2R4 and mT2R8 with 1.5 mM denatonium (e, f, h, i). No increase in $[Ca^{2+}]_i$ was observed in the absence of $G\alpha 15$ (g - i); in contrast robust $G\alpha 15$ dependent responses were observed in the presence of tastants (d - f); scales indicate $[Ca^{2+}]_i$ (nM) determined from FURA-2 emission ratios. Line traces (j - l) show the kinetics of the $[Ca^{2+}]_i$ changes for representative cells from panels (d - f); arrows indicate addition of tastants.

Figure 4 shows that mT2R5 is a taste receptor for cycloheximide. (a) HEK-293 cells expressing $G\alpha 15$ and rho-mT2R5 were challenged with multiple pulses of 2 μ M cycloheximide (CYX), 3 mM 6-n-propyl thiouracil (PROP) or 5 mM denatonium (DEN); dots and horizontal bars above the traces indicate the time and duration of tastant pulses. Cycloheximide triggers robust receptor activation. This experiment also illustrates desensitization to repeated stimulation or during sustained application of the stimulus. (b) Responses to cycloheximide are highly specific and are not observed after addition of buffer (CON) or high concentrations of other tastants. Abbreviations and concentrations used are: cycloheximide, CYX (5 μ M); atropine, ATR (5 mM); brucine, BRU (5 mM); caffeic acid, CAFF (2 mM); denatonium, DEN (5 mM); epicatechin, (-)EPI (3 mM); phenyl thiocarbamide, PTC (3 mM); 6-n-propyl thiouracil, PROP (10 mM); saccharin, SAC (10 mM); strychnine, STR (5 mM); sucrose octaacetate, SOA (3 mM). Columns represent the mean \pm s.e of at least six independent experiments. (c) The mT2R5 gene from taster (DBA/2-allele) and non-taster (C57BL/6-allele) strains mediate differential $[Ca^{2+}]_i$ changes to pulses of cycloheximide. Horizontal bars depict the time and duration of the stimulus. 200 s was allowed to elapse between stimuli to ensure that cells were not desensitized due to the successive application of cycloheximide. (d)

Cycloheximide dose-response of mT2R5. Changes in $[Ca^{2+}]_i$ are shown as FURA-2 (F340/F380) ratios normalized to the response at 30 μ M cycloheximide; points represent the mean \pm s.e. of at least six determinations. The non-taster allele shows a marked decrease in cycloheximide sensitivity relative to the taster allele (EC50s of \sim 2.3 μ M versus 0.5 μ M, respectively).

Figure 5 shows that hT2R4 and mT2R8 respond to denatonium. HEK-293 cells expressing $G\alpha_{15}$ were transiently transfected with hT2R4 or mT2R8 receptors and $[Ca^{2+}]_i$ was monitored as shown in Figure 3. (a) An increase in $[Ca^{2+}]_i$ could be induced by stimulation with denatonium but not by various other bitter compounds. Response profiles of (b) hT2R4 and (c) mT2R8 to a set of nine out of 55 different bitter and sweet tastants (see Experimental Procedures) are shown. CON refers to control buffer addition, NAR to 2mM naringin and LYS to 5mM lysine. Other abbreviations and concentrations are as reported in Figure 4. The mean FURA-2 fluorescence ratio (F340/F380) before and after ligand addition was obtained from 100 equal sized areas that included all responding cells. The values represent the mean \pm s.e. of at least 6 experiments.

Figure 6 demonstrates that cycloheximide taster and non-taster strains express different alleles of mT2R5. (a) Predicted transmembrane topology of mT2R5; amino-acid substitutions in the allele from non-taster strains are highlighted in red. The presence of only two alleles at this locus is not unexpected because the strains that share the same polymorphisms were derived from a common founder (Beck *et al.*, *Nat Genet* 24:23-55 (2000)). *In situ* hybridization showing expression of mT2R5 in subsets of cells in the circumvallate papilla of (b) a cycloheximide taster strain (DBA/2) and (c) a non-taster strain (C57BL/6); no strain specific differences in expression pattern were detected in taste buds from other regions of the oral cavity.

Figure 7 shows that mT2R5 activates gustducin in response to cycloheximide. (a) Insect larval cell membranes containing mT2R5 activate gustducin in the presence 300 μ M cycloheximide but not without ligand (control) or in the presence of 1 mM atropine, brucine, caffeine, denatonium, phenylthiocarbamide, 6-n-propyl thiouracil, quinine, saccharin, strychnine, sucrose octaacetate. (b) Cycloheximide concentration dependence of gustducin activation by mT2R5 was fitted by single-site binding ($K_d = 14.8 + 0.9 \mu$ M).

Figure 8 provides a table including nucleic acid and protein sequences for
A a number of human, rat, and mouse T2R family members. SEQ ID NO: 1-165

DETAILED DESCRIPTION OF THE INVENTION

5 I. Introduction

The present invention provides nucleic acids encoding a novel family of
taste cell specific G-protein coupled receptors. These nucleic acids and the receptors that
they encode are referred to as members of the "T2R" family of taste cell specific G
protein coupled receptors. These taste cell specific GPCRs are components of the taste
10 transduction pathway, *e.g.*, the bitter taste transduction pathway, and are involved in the
taste detection of substances such as the bitter substances 6-n-propylthiouracil (PROP),
sucrose octaacetate (soa), raffinose undecaacetate (roa), cycloheximide (cyx),
denatonium, copper glycinate (Glb), and quinine (qui).

These nucleic acids provide valuable probes for the identification of taste
15 cells, as the nucleic acids are specifically expressed in taste cells. For example, probes
for T2R polypeptides and proteins can be used to identify taste cells present in foliate,
circumvallate, and fungiform papillae, as well as taste cells present in the
geschmackstreifen and epiglottis. In particular, T2R probes are useful to identify bitter
sensing, gustducin expressing taste cells. They also serve as tools for the generation of
20 taste topographic maps that elucidate the relationship between the taste cells of the tongue
and taste sensory neurons leading to taste centers in the brain. Furthermore, the nucleic
acids and the proteins they encode can be used as probes to dissect taste-induced
behaviors.

The invention also provides methods of screening for modulators, *e.g.*,
25 activators, inhibitors, stimulators, enhancers, agonists, and antagonists, of these novel
taste cell GPCRs. Such modulators of taste transduction are useful for pharmacological
and genetic modulation of taste signaling pathways. These methods of screening can be
used to identify high affinity agonists and antagonists of taste cell activity. These
modulatory compounds can then be used in the food and pharmaceutical industries to
30 customize taste, for example, to decrease the bitter taste of foods or drugs. Thus, the
invention provides assays for taste modulation, where members of the T2R family act as
direct or indirect reporter molecules for the effect of modulators on taste transduction.
GPCRs can be used in assays, *e.g.*, to measure changes in ligand binding, ion
concentration, membrane potential, current flow, ion flux, transcription, signal

transduction, receptor-ligand interactions, second messenger concentrations, *in vitro*, *in vivo*, and *ex vivo*. In one embodiment, members of the T2R family can be used as indirect reporters via attachment to a second reporter molecule such as green fluorescent protein (see, e.g., Mistili & Spector, *Nature Biotechnology* 15:961-964 (1997)). In another
5 embodiment, T2R family members are recombinantly expressed in cells, and modulation of taste transduction via GPCR activity is assayed by measuring changes in Ca^{2+} levels and other intracellular messages such as cAMP, cGMP, and IP3.

In a preferred embodiment, a T2R polypeptide is expressed in a eukaryotic cell as a chimeric receptor with a heterologous, chaperone sequence that facilitates its
10 maturation and targeting through the secretory pathway. In a preferred embodiment, the heterologous sequence is a rhodopsin sequence, such as an N-terminal fragment of a rhodopsin. Such chimeric T2R receptors can be expressed in any eukaryotic cell, such as HEK-293 cells. Preferably, the cells comprise a functional G protein, e.g., $\text{G}\alpha_{15}$, that is capable of coupling the chimeric receptor to an intracellular signaling pathway or to a
15 signaling protein such as phospholipase $\text{C}\beta$. Activation of such chimeric receptors in such cells can be detected using any standard method, such as by detecting changes in intracellular calcium by detecting FURA-2 dependent fluorescence in the cell.

Methods of assaying for modulators of taste transduction include *in vitro* ligand binding assays using T2R polypeptides, portions thereof such as the extracellular
20 domain or transmembrane region or combination thereof, or chimeric proteins comprising one or more domains of a T2R family member; oocyte or tissue culture cell T2R gene expression, or expression of T2R fragments or fusion proteins, such as rhodopsin fusion proteins; transcriptional activation of T2R genes; phosphorylation and dephosphorylation of T2R family members; G-protein binding to GPCRs; ligand binding assays; voltage,
25 membrane potential and conductance changes; ion flux assays; changes in intracellular second messengers such as cGMP, cAMP and inositol triphosphate; changes in intracellular calcium levels; and neurotransmitter release.

Finally, the invention provides methods of detecting T2R nucleic acid and protein expression, allowing investigation of taste transduction regulation and specific
30 identification of taste receptor cells. T2R family members also provide useful nucleic acid probes for paternity and forensic investigations. T2R genes are also useful as a nucleic acid probe for identifying taste receptor cells, such as foliate, fungiform, circumvallate, geschmackstreifen, and epiglottis taste receptor cells, in particular bitter-

112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 157, 159, 161, 163, and 165, isolated from rats, mice, and humans) encodes a family of related polypeptides comprising an extracellular domain, seven transmembrane domains, and a cytoplasmic domain. Related T2R family genes from other species share at least about 60% nucleotide sequence identity over a region of at least about 50 nucleotides in length, optionally 100, 200, 500, or more nucleotides in length, to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 23, 25, 27, 29, 31, 34, 36, 38, 41, 43, 45, 52, 54, 57, 61, 63, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 157, 159, 161, 163, or 165, or encode polypeptides sharing at least about 60% amino acid sequence identity over an amino acid region at least about 25 amino acids in length, optionally 50 to 100 amino acids in length to SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 22, 24, 26, 28, 30, 32, 33, 35, 37, 39, 40, 42, 44, 46-51, 53, 55, 56, 58-60, 62, 64-77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 158, 160, 162, or 164. T2R genes are specifically expressed in taste cells.

Several consensus amino acid sequences or domains have also been identified that are characteristic of T2R family members. For example, T2R family members typically comprise a sequence having at least about 50%, optionally 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or higher, identity to SEQ ID NO: 166 (corresponding, *e.g.*, to amino acid positions 16-35 in SEQ ID NO: 1, and to T2R transmembrane region 1), SEQ ID NO: 167 (corresponding, *e.g.*, to amino acid positions 45-58 in SEQ ID NO: 1, and to T2R transmembrane region 2), SEQ ID NO: 168 (corresponding, *e.g.*, to amino acid positions 89-101 in SEQ ID NO: 1, and to T2R transmembrane region 3), SEQ ID NO: 169 (corresponding, *e.g.*, to amino acid positions 102-119 in SEQ ID NO: 1, and to T2R transmembrane region ⁴~~β~~), SEQ ID NO: 170 (corresponding, *e.g.*, to amino acid positions 196-209 in SEQ ID NO: 1, and to T2R transmembrane region 5), or SEQ ID NO: 171 (corresponding, *e.g.*, to amino acid positions 273-286 in SEQ ID NO: 35, and to T2R transmembrane region 7). These conserved domains thus can be used to identify members of the T2R family, by % identity, specific hybridization or amplification, or specific binding by antibodies raised against a domain.

Several T2R genes represent apparent orthologs of each other. For example, human T2R01 (SEQ ID NOs:1, 2), rat T2R01 (SEQ ID NOs:77, 78), and mouse T2R19 (SEQ ID NOs:141, 142), are apparent orthologs. In addition, rat T2R08 (SEQ ID NOs:91, 92) and mouse T2R02 (SEQ ID NOs:107, 108) are about 74% identical at the amino acid sequence level, and are each at least about 50% identical to human T2R13 (SEQ ID NOs:24, 25). Rat T2R03 (SEQ ID NOs:81, 82) and mouse T2R18 (SEQ ID NOs:139, 140) are about 92% identical, and are each at least about 50% identical to human T2R16 (SEQ ID NOs:30, 31). Finally, human T2R04 (SEQ ID NOs:7, 8) and mouse T2R08 (SEQ ID NOs:119, 120) are about 67% identical to each other.

The present invention also provides polymorphic variants of the T2R proteins provided herein. For example, in the rat T2R depicted in SEQ ID NO:77: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 7; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 20.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:79: variant #1, in which a tyrosine residue is substituted for a phenylalanine residue at amino acid position 2; and variant #2, in which a valine residue is substituted for an isoleucine residue at amino acid position 62.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:81: variant #1, in which a glutamine residue is substituted for an asparagine residue at amino acid position 179; and variant #2, in which a cysteine residue is substituted for a methionine residue at amino acid position 183.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:83: variant #1, in which a glycine residue is substituted for an alanine residue at amino acid position 4; and variant #2, in which a leucine residue is substituted for an isoleucine residue at amino acid position 63.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:85: variant #1, in which a valine residue is substituted for an isoleucine residue at amino acid position 56; and variant #2, in which a methionine residue is substituted for a cysteine residue at amino acid position 57.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:87: variant #1, in which an isoleucine residue is substituted for a valine residue at amino acid position 4; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 5.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:89: variant #1, in which an alanine residue is substituted for a glycine residue at amino acid position 79; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 127.

5 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:91: variant #1, in which a leucine residue is substituted for a valine residue at amino acid position 28; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 80.

10 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:93: variant #1, in which an arginine residue is substituted for a lysine residue at amino acid position 75; and variant #2, in which a methionine residue is substituted for a cysteine residue at amino acid position 251.

15 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:95: variant #1, in which a threonine residue is substituted for a serine residue at amino acid position 48; and variant #2, in which an isoleucine residue is substituted for a valine residue at amino acid position 49.

20 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:97: variant #1, in which a glutamic acid residue is substituted for an aspartic acid residue at amino acid position 25; and variant #2, in which an isoleucine residue is substituted for a leucine residue at amino acid position 100.

 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:99: variant #1, in which a serine residue is substituted for a threonine residue at amino acid position 4; and variant #2, in which an isoleucine residue is substituted for a valine residue at amino acid position 74.

25 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:101: variant #1, in which an asparagine residue is substituted for a glutamine residue at amino acid position 9; and variant #2, in which a tryptophan residue is substituted for a tyrosine residue at amino acid position 18.

30 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:103: variant #1, in which a threonine residue is substituted for a serine residue at amino acid position 26; and variant #2, in which an isoleucine residue is substituted for a valine residue at amino acid position 8.

 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:105: variant #1, in which an isoleucine residue is

substituted for a leucine residue at amino acid position 4; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 46.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:107: variant #1, in which a threonine residue is substituted for a serine residue at amino acid position 3; and variant #2, in which an isoleucine residue is substituted for a valine residue at amino acid position 28.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:109: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 26; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 50.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:111: variant #1, in which a glycine residue is substituted for an alanine residue at amino acid position 4; and variant #2, in which a phenylalanine residue is substituted for a tryptophan residue at amino acid position 60.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:113: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 62; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 244.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:115: variant #1, in which a serine residue is substituted for a threonine residue at amino acid position 3; and variant #2, in which a lysine residue is substituted for an arginine residue at amino acid position 123.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:117: variant #1, in which an asparagine residue is substituted for a glutamine residue at amino acid position 65; and variant #2, in which a leucine residue is substituted for an isoleucine residue at amino acid position 68.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:119: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 2; and variant #2, in which an aspartic acid residue is substituted for a glutamic acid residue at amino acid position 4.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:121: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 16; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 46.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:123: variant #1, in which a threonine residue is substituted for a serine residue at amino acid position 9; and variant #2, in which a tryptophan residue is substituted for a phenylalanine residue at amino acid position 14.

5 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:125: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 24; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 53.

10 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:127: variant #1, in which a phenylalanine residue is substituted for a tryptophan residue at amino acid position 51; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 101.

15 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:129: variant #1, in which an isoleucine residue is substituted for a valine residue at amino acid position 4; and variant #2, in which a glycine residue is substituted for an alanine residue at amino acid position 52.

20 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:131: variant #1, in which an arginine residue is substituted for a lysine residue at amino acid position 150; and variant #2, in which a leucine residue is substituted for a valine residue at amino acid position 225.

25 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:133: variant #1, in which a leucine residue is substituted for an isoleucine residue at amino acid position 27; and variant #2, in which a lysine residue is substituted for an arginine residue at amino acid position 127.

30 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:135: variant #1, in which a threonine residue is substituted for a serine residue at amino acid position 102; and variant #2, in which a glutamic acid residue is substituted for an aspartic acid residue at amino acid position 220.

 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:137: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 24; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 45.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:139: variant #1, in which a leucine residue is substituted for an isoleucine residue at amino acid position 50; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 53.

5 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:141: variant #1, in which a serine residue is substituted for a threonine residue at amino acid position 76; and variant #2, in which an isoleucine residue is substituted for a leucine residue at amino acid position 131.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:143: variant #1, in which an alanine residue is substituted for a glycine residue at amino acid position 98; and variant #2, in which a phenylalanine residue is substituted for a tryptophan residue at amino acid position 153.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:145: variant #1, in which a leucine residue is substituted for an isoleucine residue at amino acid position 8; and variant #2, in which a glycine residue is substituted for an alanine residue at amino acid position 100.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:147: variant #1, in which a glycine residue is substituted for an alanine residue at amino acid position 52; and variant #2, in which a valine residue is substituted for a leucine residue at amino acid position 75.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:149: variant #1, in which a lysine residue is substituted for an arginine residue at amino acid position 44; and variant #2, in which a leucine residue is substituted for a valine residue at amino acid position 49.

25 The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:151: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 5; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 25.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:153: variant #1, in which a glutamic acid residue is substituted for an aspartic acid residue at amino acid position 7; and variant #2, in which an isoleucine residue is substituted for a leucine residue at amino acid position 60.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:155: variant #1, in which an isoleucine residue is

substituted for a valine residue at amino acid position 7; and variant #2, in which a glycine residue is substituted for an alanine residue at amino acid position 23.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:158: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 5; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 21.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:160: variant #1, in which a leucine residue is substituted for a valine residue at amino acid position 5; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 23.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:162: variant #1, in which an isoleucine residue is substituted for a leucine residue at amino acid position 22; and variant #2, in which an alanine residue is substituted for a glycine residue at amino acid position 34.

The present invention also provides polymorphic variants of the T2R protein depicted in SEQ ID NO:164: variant #1, in which a leucine residue is substituted for an isoleucine residue at amino acid position 49; and variant #2, in which an arginine residue is substituted for a lysine residue at amino acid position 76.

Specific regions of the T2R nucleotide and amino acid sequences may be used to identify polymorphic variants, interspecies homologs, and alleles of T2R family members. This identification can be made *in vitro*, *e.g.*, under stringent hybridization conditions or PCR (*e.g.*, using primers encoding SEQ ID NOS:166-171) and sequencing, or by using the sequence information in a computer system for comparison with other nucleotide sequences. Typically, identification of polymorphic variants and alleles of T2R family members is made by comparing an amino acid sequence of about 25 amino acids or more, *e.g.*, 50-100 amino acids. Amino acid identity of approximately at least 60% or above, optionally 65%, 70%, 75%, 80%, 85%, or 90-95% or above typically demonstrates that a protein is a polymorphic variant, interspecies homolog, or allele of a T2R family member. Sequence comparison can be performed using any of the sequence comparison algorithms discussed below. Antibodies that bind specifically to T2R polypeptides or a conserved region thereof can also be used to identify alleles, interspecies homologs, and polymorphic variants.

Polymorphic variants, interspecies homologs, and alleles of T2R genes are confirmed by examining taste cell specific expression of the putative T2R polypeptide.

Typically, T2R polypeptides having an amino acid sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, or SEQ ID NO:164 is used as a positive control in comparison to the putative T2R protein to demonstrate the identification of a polymorphic variant or allele of the T2R family member. The polymorphic variants, alleles and interspecies homologs are expected to retain the seven transmembrane structure of a G-protein coupled receptor.

The present invention also provides nucleotide sequences for T2R promoters, which can be used to drive taste cell-specific expression of polynucleotides, especially in gustducin expressing taste cells that are receptive to bitter tastants.

Nucleotide and amino acid sequence information for T2R family members may also be used to construct models of taste cell specific polypeptides in a computer system. These models are subsequently used to identify compounds that can activate or inhibit T2R receptor proteins. Such compounds that modulate the activity of T2R family members can be used to investigate the role of T2R genes in taste transduction.

The isolation of T2R family members provides a means for assaying for inhibitors and activators of G-protein coupled receptor taste transduction. Biologically active T2R proteins are useful for testing inhibitors and activators of T2R as taste

transducers, especially bitter taste transducers, using *in vivo* and *in vitro* assays that measure, *e.g.*, transcriptional activation of T2R-dependent genes; ligand binding; phosphorylation and dephosphorylation; binding to G-proteins; G-protein activation; regulatory molecule binding; voltage, membrane potential and conductance changes; ion flux; intracellular second messengers such as cGMP, cAMP and inositol triphosphate; intracellular calcium levels; and neurotransmitter release. Such activators and inhibitors identified using T2R family members can be used to further study taste transduction and to identify specific taste agonists and antagonists. Such activators and inhibitors are useful as pharmaceutical and food agents for customizing taste, for example to decrease the bitter taste of foods or pharmaceuticals.

The present invention also provides assays, preferably high throughput assays, to identify molecules that interact with and/or modulate a T2R polypeptide. In numerous assays, a particular domain of a T2R family member is used, *e.g.*, an extracellular, transmembrane, or intracellular domain or region. In numerous embodiments, an extracellular domain or transmembrane region or combination thereof is bound to a solid substrate, and used, *e.g.*, to isolate ligands, agonists, antagonists, or any other molecule that can bind to and/or modulate the activity of an extracellular domain or transmembrane region of a T2R polypeptide. In certain embodiments, a domain of a T2R polypeptide, *e.g.*, an extracellular, transmembrane, or intracellular domain, is fused to a heterologous polypeptide, thereby forming a chimeric polypeptide, *e.g.*, a chimeric polypeptide with G protein coupled receptor activity. Such chimeric polypeptides are useful, *e.g.*, in assays to identify ligands, agonists, antagonists, or other modulators of a T2R polypeptide. In addition, such chimeric polypeptides are useful to create novel taste receptors with novel ligand binding specificity, modes of regulation, signal transduction pathways, or other such properties, or to create novel taste receptors with novel combinations of ligand binding specificity, modes of regulation, signal transduction pathways, *etc.*

Methods of detecting T2R nucleic acids and expression of T2R polypeptides are also useful for identifying taste cells and creating topological maps of the tongue and the relation of tongue taste receptor cells to taste sensory neurons in the brain. In particular, methods of detecting T2R can be used to identify taste cells sensitive to bitter tastants. Chromosome localization of the genes encoding human T2R genes can be used to identify diseases, mutations, and traits caused by and associated with T2R family members.

II. Definitions

As used herein, the following terms have the meanings ascribed to them unless specified otherwise.

5 “Taste cells” include neuroepithelial cells that are organized into groups to form taste buds of the tongue, *e.g.*, foliate, fungiform, and circumvallate cells (*see, e.g.*, Roper *et al.*, *Ann. Rev. Neurosci.* 12:329-353 (1989)). Taste cells also include cells of the palate, and other tissues that may contain taste cells such as the esophagus and the stomach.

10 “T2R” refers to one or more members of a family of G-protein coupled receptors that are expressed in taste cells such as foliate, fungiform, and circumvallate cells, as well as cells of the palate, esophagus, and stomach (*see, e.g.*, Hoon *et al.*, *Cell* 96:541-551 (1999), herein incorporated by reference in its entirety). This family is also referred to as the “SF family” (*see, e.g.*, USSN 09/393,634). Such taste cells can be
15 identified because they express specific molecules such as Gustducin, a taste cell specific G protein, or other taste specific molecules (McLaughlin *et al.*, *Nature* 357:563-569 (1992)). Taste receptor cells can also be identified on the basis of morphology (*see, e.g.*, Roper, *supra*). T2R family members have the ability to act as receptors for taste transduction. T2R family members are also referred to as the “GR” family, for gustatory
20 receptor, or “SF” family.

 “T2R” nucleic acids encode a family of GPCRs with seven transmembrane regions that have “G-protein coupled receptor activity,” *e.g.*, they bind to G-proteins in response to extracellular stimuli and promote production of second messengers such as IP3, cAMP, cGMP, and Ca²⁺ via stimulation of enzymes such as phospholipase C and
25 adenylylate cyclase (for a description of the structure and function of GPCRs, *see, e.g.*, Fong, *supra*, and Baldwin, *supra*). A dendogram providing the relationship between certain T2R family members is provided as Figure 2. These nucleic acids encode proteins that are expressed in taste cells, in particular Gustducin-expressing taste cells that are responsive to bitter tastants. A single taste cell may contain many distinct T2R
30 polypeptides.

 The term “T2R” family therefore refers to polymorphic variants, alleles, mutants, and interspecies homologs that: (1) have about 60% amino acid sequence identity, optionally about 75, 80, 85, 90, or 95% amino acid sequence identity to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ

ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID
 NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID
 NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID
 NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID
 5 NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID
 NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID
 NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID
 NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID
 NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID
 10 NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID
 NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID
 NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID
 NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID
 NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID
 15 NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID
 NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID
 NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID
 NO:160, SEQ ID NO:162, or SEQ ID NO:164 over a window of about 25 amino acids,
 optionally 50-100 amino acids; (2) specifically bind to antibodies raised against an
 20 immunogen comprising an amino acid sequence selected from the group consisting of
 SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID
 NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID
 NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID
 NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID
 25 NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID
 NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID
 NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID
 NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID
 NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID
 30 NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID
 NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID
 NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID
 NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID
 NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID

NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID
 NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID
 NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID
 NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID
 5 NO:158, SEQ ID NO:160, SEQ ID NO:162, and SEQ ID NO:164, and conservatively
 modified variants thereof; (3) specifically hybridize (with a size of at least about 100,
 optionally at least about 500-1000 nucleotides) under stringent hybridization conditions to
 a sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID
 NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16,
 10 SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ
 ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID
 NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID
 NO:57, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:78, SEQ ID NO:80, SEQ ID
 NO:82, SEQ ID NO:84, SEQ ID NO:86, SEQ ID NO:88, SEQ ID NO:90, SEQ ID
 15 NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID
 NO:102, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID
 NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, ~~SEQ ID~~
~~NO:120~~, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID
 NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID
 20 NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID
 NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID
 NO:159, SEQ ID NO:161, SEQ ID NO:163, and SEQ ID NO:165, and conservatively
 modified variants thereof; (4) comprise a sequence at least about 50% identical to an
 amino acid sequence selected from the group consisting of SEQ ID NO:166, SEQ ID
 25 NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:171; or
 (5) are amplified by primers that specifically hybridize under stringent hybridization
 conditions to the same sequence as a degenerate primer sets encoding SEQ ID NO:166,
 SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, or SEQ ID
 NO:171.

30 Topologically, sensory GPCRs have an "N-terminal domain"
 "extracellular domains," a "transmembrane domain" comprising seven transmembrane
 regions, cytoplasmic, and extracellular loops, "cytoplasmic domains," and a "C-terminal
 domain" (*see, e.g., Hoon et al., Cell* 96:541-551 (1999); Buck & Axel, *Cell* 65:175-187
 (1991)). These domains can be structurally identified using methods known to those of

skill in the art, such as sequence analysis programs that identify hydrophobic and hydrophilic domains (*see, e.g., Stryer, Biochemistry* (3rd ed. 1988); *see also* any of a number of Internet based sequence analysis programs, such as those found at dot.imgen.bcm.tmc.edu). Such domains are useful for making chimeric proteins and for
5 *in vitro* assays of the invention, *e.g.,* ligand binding assays.

“Extracellular domains” therefore refers to the domains of T2R polypeptides that protrude from the cellular membrane and are exposed to the extracellular face of the cell. Such domains would include the “N terminal domain” that is exposed to the extracellular face of the cell, as well as the extracellular loops of the
10 transmembrane domain that are exposed to the extracellular face of the cell, *i.e.,* the loops between transmembrane regions 2 and 3, and between transmembrane regions 4 and 5. The “N terminal domain” region starts at the N-terminus and extends to a region close to the start of the transmembrane domain. These extracellular domains are useful for *in vitro* ligand binding assays, both soluble and solid phase. In addition, transmembrane
15 regions, described below, can also bind ligand either in combination with the extracellular domain or alone, and are therefore also useful for *in vitro* ligand binding assays.

“Transmembrane domain,” which comprises the seven transmembrane “regions,” refers to the domain of T2R polypeptides that lies within the plasma membrane, and may also include the corresponding cytoplasmic (intracellular) and
20 extracellular loops, also referred to as transmembrane domain “regions.” The seven transmembrane regions and extracellular and cytoplasmic loops can be identified using standard methods, as described in Kyte & Doolittle, *J. Mol. Biol.* 157:105-132 (1982)), or in Stryer, *supra*.

“Cytoplasmic domains” refers to the domains of T2R proteins that face the
25 inside of the cell, *e.g.,* the “C terminal domain” and the intracellular loops of the transmembrane domain, *e.g.,* the intracellular loops between transmembrane regions 1 and 2, and the intracellular loops between transmembrane regions 3 and 4. “C terminal domain” refers to the region that spans the end of the last transmembrane domain and the C-terminus of the protein, and which is normally located within the cytoplasm.

“Biological sample” as used herein is a sample of biological tissue or fluid
30 that contains one or more T2R nucleic acids encoding one or more T2R proteins. Such samples include, but are not limited to, tissue isolated from humans, mice, and rats, in particular, tongue, palate, and other tissues that may contain taste cells such as the esophagus and the stomach. Biological samples may also include sections of tissues such

as frozen sections taken for histological purposes. A biological sample is typically obtained from a eukaryotic organism, such as insects, protozoa, birds, fish, reptiles, and preferably a mammal such as rat, mouse, cow, dog, guinea pig, or rabbit, and most preferably a primate such as chimpanzees or humans.

5 “GPCR activity” refers to the ability of a GPCR to transduce a signal. Such activity can be measured in a heterologous cell, by coupling a GPCR (or a chimeric GPCR) to either a G-protein or promiscuous G-protein such as Gα15, and an enzyme such as PLC, and measuring increases in intracellular calcium using (Offermans & Simon, *J. Biol. Chem.* 270:15175-15180 (1995)). Receptor activity can be effectively
10 measured by recording ligand-induced changes in $[Ca^{2+}]_i$ using fluorescent Ca^{2+} -indicator dyes and fluorometric imaging. Optionally, the polypeptides of the invention are involved in sensory transduction, optionally taste transduction in taste cells.

 The phrase “functional effects” in the context of assays for testing compounds that modulate T2R family member mediated taste transduction includes the
15 determination of any parameter that is indirectly or directly under the influence of the receptor, *e.g.*, functional, physical and chemical effects. It includes ligand binding, changes in ion flux, membrane potential, current flow, transcription, G-protein binding, GPCR phosphorylation or dephosphorylation, signal transduction, receptor-ligand interactions, second messenger concentrations (*e.g.*, cAMP, cGMP, IP3, or intracellular
20 Ca^{2+}), *in vitro*, *in vivo*, and *ex vivo* and also includes other physiologic effects such increases or decreases of neurotransmitter or hormone release.

 By “determining the functional effect” is meant assays for a compound that increases or decreases a parameter that is indirectly or directly under the influence of a T2R family member, *e.g.*, functional, physical and chemical effects. Such functional
25 effects can be measured by any means known to those skilled in the art, *e.g.*, changes in spectroscopic characteristics (*e.g.*, fluorescence, absorbance, refractive index), hydrodynamic (*e.g.*, shape), chromatographic, or solubility properties, patch clamping, voltage-sensitive dyes, whole cell currents, radioisotope efflux, inducible markers, oocyte T2R gene expression; tissue culture cell T2R expression; transcriptional activation of
30 T2R genes; ligand binding assays; voltage, membrane potential and conductance changes; ion flux assays; changes in intracellular second messengers such as cAMP, cGMP, and inositol triphosphate (IP3); changes in intracellular calcium levels; neurotransmitter release, and the like.

“Inhibitors,” “activators,” and “modulators” of T2R genes or proteins are used interchangeably to refer to inhibitory, activating, or modulating molecules identified using *in vitro* and *in vivo* assays for taste transduction, *e.g.*, ligands, agonists, antagonists, and their homologs and mimetics. Inhibitors are compounds that, *e.g.*, bind to, partially or totally block stimulation, decrease, prevent, delay activation, inactivate, desensitize, or down regulate taste transduction, *e.g.*, antagonists. Activators are compounds that, *e.g.*, bind to, stimulate, increase, open, activate, facilitate, enhance activation, sensitize or up regulate taste transduction, *e.g.*, agonists. Modulators include compounds that, *e.g.*, alter the interaction of a receptor with: extracellular proteins that bind activators or inhibitor (*e.g.*, ebnerin and other members of the hydrophobic carrier family); G -proteins; kinases (*e.g.*, homologs of rhodopsin kinase and beta adrenergic receptor kinases that are involved in deactivation and desensitization of a receptor); and arrestin-like proteins, which also deactivate and desensitize receptors. Modulators include genetically modified versions of T2R family members, *e.g.*, with altered activity, as well as naturally occurring and synthetic ligands, antagonists, agonists, small chemical molecules and the like. Such assays for inhibitors and activators include, *e.g.*, expressing T2R family members in cells or cell membranes, applying putative modulator compounds, in the presence or absence of tastants, *e.g.*, bitter tastants, and then determining the functional effects on taste transduction, as described above. Samples or assays comprising T2R family members that are treated with a potential activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of inhibition. Control samples (untreated with inhibitors) are assigned a relative T2R activity value of 100%. Inhibition of a T2R is achieved when the T2R activity value relative to the control is about 80%, optionally 50% or 25-0%. Activation of a T2R is achieved when the T2R activity value relative to the control is 110%, optionally 150%, optionally 200-500%, or 1000-3000% higher.

“Biologically active” T2R refers to a T2R having GPCR activity as described above, involved in taste transduction in taste receptor cells, in particular bitter taste transduction.

The terms “isolated” “purified” or “biologically pure” refer to material that is substantially or essentially free from components which normally accompany it as found in its native state. Purity and homogeneity are typically determined using analytical chemistry techniques such as polyacrylamide gel electrophoresis or high performance liquid chromatography. A protein that is the predominant species present in

acid, *i.e.*, an α carbon that is bound to a hydrogen, a carboxyl group, an amino group, and an R group, *e.g.*, homoserine, norleucine, methionine sulfoxide, methionine methyl sulfonium. Such analogs have modified R groups (*e.g.*, norleucine) or modified peptide backbones, but retain the same basic chemical structure as a naturally occurring amino acid. Amino acid mimetics refers to chemical compounds that have a structure that is different from the general chemical structure of an amino acid, but that functions in a manner similar to a naturally occurring amino acid.

Amino acids may be referred to herein by either their commonly known three letter symbols or by the one-letter symbols recommended by the IUPAC-IUB Biochemical Nomenclature Commission. Nucleotides, likewise, may be referred to by their commonly accepted single-letter codes.

“Conservatively modified variants” applies to both amino acid and nucleic acid sequences. With respect to particular nucleic acid sequences, conservatively modified variants refers to those nucleic acids which encode identical or essentially identical amino acid sequences, or where the nucleic acid does not encode an amino acid sequence, to essentially identical sequences. Because of the degeneracy of the genetic code, a large number of functionally identical nucleic acids encode any given protein. For instance, the codons GCA, GCC, GCG and GCU all encode the amino acid alanine. Thus, at every position where an alanine is specified by a codon, the codon can be altered to any of the corresponding codons described without altering the encoded polypeptide. Such nucleic acid variations are “silent variations,” which are one species of conservatively modified variations. Every nucleic acid sequence herein which encodes a polypeptide also describes every possible silent variation of the nucleic acid. One of skill will recognize that each codon in a nucleic acid (except AUG, which is ordinarily the only codon for methionine, and TGG, which is ordinarily the only codon for tryptophan) can be modified to yield a functionally identical molecule. Accordingly, each silent variation of a nucleic acid which encodes a polypeptide is implicit in each described sequence.

As to amino acid sequences, one of skill will recognize that individual substitutions, deletions or additions to a nucleic acid, peptide, polypeptide, or protein sequence which alters, adds or deletes a single amino acid or a small percentage of amino acids in the encoded sequence is a “conservatively modified variant” where the alteration results in the substitution of an amino acid with a chemically similar amino acid. Conservative substitution tables providing functionally similar amino acids are well

known in the art. Such conservatively modified variants are in addition to and do not exclude polymorphic variants, interspecies homologs, and alleles of the invention.

The following eight groups each contain amino acids that are conservative substitutions for one another:

- 5 1) Alanine (A), Glycine (G);
 - 2) Aspartic acid (D), Glutamic acid (E);
 - 3) Asparagine (N), Glutamine (Q);
 - 4) Arginine (R), Lysine (K);
 - 5) Isoleucine (I), Leucine (L), Methionine (M), Valine (V);
 - 10 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W);
 - 7) Serine (S), Threonine (T); and
 - 8) Cysteine (C), Methionine (M)
- (see, e.g., Creighton, *Proteins* (1984)).

Macromolecular structures such as polypeptide structures can be described
15 in terms of various levels of organization. For a general discussion of this organization, see, e.g., Alberts *et al.*, *Molecular Biology of the Cell* (3rd ed., 1994) and Cantor and Schimmel, *Biophysical Chemistry Part I: The Conformation of Biological Macromolecules* (1980). “Primary structure” refers to the amino acid sequence of a particular peptide. “Secondary structure” refers to locally ordered, three dimensional
20 structures within a polypeptide. These structures are commonly known as domains. Domains are portions of a polypeptide that form a compact unit of the polypeptide and are typically 50 to 350 amino acids long. Typical domains are made up of sections of lesser organization such as stretches of β -sheet and α -helices. “Tertiary structure” refers to the complete three dimensional structure of a polypeptide monomer. “Quaternary
25 structure” refers to the three dimensional structure formed by the noncovalent association of independent tertiary units. Anisotropic terms are also known as energy terms.

A “label” or a “detectable moiety” is a composition detectable by spectroscopic, photochemical, biochemical, immunochemical, or chemical means. For example, useful labels include ³²P, fluorescent dyes, electron-dense reagents, enzymes
30 (e.g., as commonly used in an ELISA), biotin, digoxigenin, or haptens and proteins which can be made detectable, e.g., by incorporating a radiolabel into the peptide or used to detect antibodies specifically reactive with the peptide.

A "labeled nucleic acid probe or oligonucleotide" is one that is bound, either covalently, through a linker or a chemical bond, or noncovalently, through ionic, van der Waals, electrostatic, or hydrogen bonds to a label such that the presence of the probe may be detected by detecting the presence of the label bound to the probe.

5 As used herein a "nucleic acid probe or oligonucleotide" is defined as a nucleic acid capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing, usually through hydrogen bond formation. As used herein, a probe may include natural (*i.e.*, A, G, C, or T) or modified bases (7-deazaguanosine, inosine, *etc.*). In
10 addition, the bases in a probe may be joined by a linkage other than a phosphodiester bond, so long as it does not interfere with hybridization. Thus, for example, probes may be peptide nucleic acids in which the constituent bases are joined by peptide bonds rather than phosphodiester linkages. It will be understood by one of skill in the art that probes may bind target sequences lacking complete complementarity with the probe sequence
15 depending upon the stringency of the hybridization conditions. The probes are optionally directly labeled as with isotopes, chromophores, lumiphores, chromogens, or indirectly labeled such as with biotin to which a streptavidin complex may later bind. By assaying for the presence or absence of the probe, one can detect the presence or absence of the select sequence or subsequence.

20 The term "recombinant" when used with reference, *e.g.*, to a cell, or nucleic acid, protein, or vector, indicates that the cell, nucleic acid, protein or vector, has been modified by the introduction of a heterologous nucleic acid or protein or the alteration of a native nucleic acid or protein, or that the cell is derived from a cell so modified. Thus, for example, recombinant cells express genes that are not found within
25 the native (non-recombinant) form of the cell or express native genes that are otherwise abnormally expressed, under expressed or not expressed at all.

The term "heterologous" when used with reference to portions of a nucleic acid indicates that the nucleic acid comprises two or more subsequences that are not found in the same relationship to each other in nature. For instance, the nucleic acid is
30 typically recombinantly produced, having two or more sequences from unrelated genes arranged to make a new functional nucleic acid, *e.g.*, a promoter from one source and a coding region from another source. Similarly, a heterologous protein indicates that the protein comprises two or more subsequences that are not found in the same relationship to each other in nature (*e.g.*, a fusion protein).

A “promoter” is defined as an array of nucleic acid control sequences that direct transcription of a nucleic acid. As used herein, a promoter includes necessary nucleic acid sequences near the start site of transcription, such as, in the case of a polymerase II type promoter, a TATA element. A promoter also optionally includes
5 distal enhancer or repressor elements, which can be located as much as several thousand base pairs from the start site of transcription. A “constitutive” promoter is a promoter that is active under most environmental and developmental conditions. An “inducible” promoter is a promoter that is active under environmental or developmental regulation. The term “operably linked” refers to a functional linkage between a nucleic acid
10 expression control sequence (such as a promoter, or array of transcription factor binding sites) and a second nucleic acid sequence, wherein the expression control sequence directs transcription of the nucleic acid corresponding to the second sequence.

An “expression vector” is a nucleic acid construct, generated recombinantly or synthetically, with a series of specified nucleic acid elements that
15 permit transcription of a particular nucleic acid in a host cell. The expression vector can be part of a plasmid, virus, or nucleic acid fragment. Typically, the expression vector includes a nucleic acid to be transcribed operably linked to a promoter.

The terms “identical” or percent “identity,” in the context of two or more nucleic acids or polypeptide sequences, refer to two or more sequences or subsequences
20 or domains that are the same or have a specified percentage of amino acid residues or nucleotides that are the same (*i.e.*, 50% identity, optionally 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or higher identity over a specified region), when compared and aligned for maximum correspondence over a comparison window, or designated region as measured using one of the following sequence comparison algorithms or by manual
25 alignment and visual inspection. Such sequences are then said to be “substantially identical.” This definition also refers to the complement of a test sequence. Optionally, the identity exists over a region that is at least about 50 amino acids or nucleotides in length, or more preferably over a region that is 75-100 amino acids or nucleotides in length.

30 For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Default program parameters can be used, as described below for the

BLASTN and BLASTP programs, or alternative parameters can be designated. The sequence comparison algorithm then calculates the percent sequence identities for the test sequences relative to the reference sequence, based on the program parameters.

A "comparison window", as used herein, includes reference to a segment of any one of the number of contiguous positions selected from the group consisting of from 20 to 600, usually about 50 to about 200, more usually about 100 to about 150 in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Methods of alignment of sequences for comparison are well-known in the art. Optimal alignment of sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith & Waterman, *Adv. Appl. Math.* 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, *J. Mol. Biol.* 48:443 (1970), by the search for similarity method of Pearson & Lipman, *Proc. Nat'l. Acad. Sci. USA* 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by manual alignment and visual inspection (*see, e.g., Current Protocols in Molecular Biology* (Ausubel *et al.*, eds. 1995 supplement)).

A preferred example of an algorithm that is suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al.*, *Nuc. Acids Res.* 25:3389-3402 (1977) and Altschul *et al.*, *J. Mol. Biol.* 215:403-410 (1990), respectively. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al.*, *supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by

the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for
5 nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (*see* Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915 (1989)) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a
10 comparison of both strands.

Another example of a useful algorithm is PILEUP. PILEUP creates a multiple sequence alignment from a group of related sequences using progressive, pairwise alignments to show relationship and percent sequence identity. It also plots a tree or dendrogram showing the clustering relationships used to create the alignment (*see*,
15 *e.g.*, Figure 2). PILEUP uses a simplification of the progressive alignment method of Feng & Doolittle, *J. Mol. Evol.* 35:351-360 (1987). The method used is similar to the method described by Higgins & Sharp, *CABIOS* 5:151-153 (1989). The program can align up to 300 sequences, each of a maximum length of 5,000 nucleotides or amino acids. The multiple alignment procedure begins with the pairwise alignment of the two
20 most similar sequences, producing a cluster of two aligned sequences. This cluster is then aligned to the next most related sequence or cluster of aligned sequences. Two clusters of sequences are aligned by a simple extension of the pairwise alignment of two individual sequences. The final alignment is achieved by a series of progressive, pairwise alignments. The program is run by designating specific sequences and their amino acid
25 or nucleotide coordinates for regions of sequence comparison and by designating the program parameters. Using PILEUP, a reference sequence is compared to other test sequences to determine the percent sequence identity relationship using the following parameters: default gap weight (3.00), default gap length weight (0.10), and weighted end gaps. PILEUP can be obtained from the GCG sequence analysis software package, *e.g.*,
30 version 7.0 (Devereaux *et al.*, *Nuc. Acids Res.* 12:387-395 (1984)).

An indication that two nucleic acid sequences or polypeptides are substantially identical is that the polypeptide encoded by the first nucleic acid is immunologically cross reactive with the antibodies raised against the polypeptide encoded by the second nucleic acid, as described below. Thus, a polypeptide is typically

substantially identical to a second polypeptide, for example, where the two peptides differ only by conservative substitutions. Another indication that two nucleic acid sequences are substantially identical is that the two molecules or their complements hybridize to each other under stringent conditions, as described below. Yet another indication that two nucleic acid sequences are substantially identical is that the same primers can be used to amplify the sequence.

The phrase “selectively (or specifically) hybridizes to” refers to the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent hybridization conditions when that sequence is present in a complex mixture (*e.g.*, total cellular or library DNA or RNA).

The phrase “stringent hybridization conditions” refers to conditions under which a probe will hybridize to its target subsequence, typically in a complex mixture of nucleic acid, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures. An extensive guide to the hybridization of nucleic acids is found in Tijssen, *Techniques in Biochemistry and Molecular Biology--Hybridization with Nucleic Probes*, “Overview of principles of hybridization and the strategy of nucleic acid assays” (1993). Generally, stringent conditions are selected to be about 5-10° C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength pH. The T_m is the temperature (under defined ionic strength, pH, and nucleic concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at T_m , 50% of the probes are occupied at equilibrium). Stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30° C for short probes (*e.g.*, 10 to 50 nucleotides) and at least about 60° C for long probes (*e.g.*, greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. For selective or specific hybridization, a positive signal is at least two times background, optionally 10 times background hybridization. Exemplary stringent hybridization conditions can be as following: 50% formamide, 5x SSC, and 1% SDS, incubating at 42°C, or, 5x SSC, 1% SDS, incubating at 65°C, with wash in 0.2x SSC, and 0.1% SDS at 65°C. Such hybridizations and wash steps can be carried out for, *e.g.*, 1, 2, 5, 10, 15, 30, 60, or more minutes.

methodology. Thus, the term antibody, as used herein, also includes antibody fragments either produced by the modification of whole antibodies, or those synthesized *de novo* using recombinant DNA methodologies (*e.g.*, single chain Fv) or those identified using phage display libraries (*see, e.g.*, McCafferty *et al.*, *Nature* 348:552-554 (1990)).

5 For preparation of monoclonal or polyclonal antibodies, any technique known in the art can be used (*see, e.g.*, Kohler & Milstein, *Nature* 256:495-497 (1975); Kozbor *et al.*, *Immunology Today* 4: 72 (1983); Cole *et al.*, pp. 77-96 in *Monoclonal Antibodies and Cancer Therapy* (1985)). Techniques for the production of single chain antibodies (U.S. Patent 4,946,778) can be adapted to produce antibodies to polypeptides
10 of this invention. Also, transgenic mice, or other organisms such as other mammals, may be used to express humanized antibodies. Alternatively, phage display technology can be used to identify antibodies and heteromeric Fab fragments that specifically bind to selected antigens (*see, e.g.*, McCafferty *et al.*, *Nature* 348:552-554 (1990); Marks *et al.*, *Biotechnology* 10:779-783 (1992)).

15 A “chimeric antibody” is an antibody molecule in which (a) the constant region, or a portion thereof, is altered, replaced or exchanged so that the antigen binding site (variable region) is linked to a constant region of a different or altered class, effector function and/or species, or an entirely different molecule which confers new properties to the chimeric antibody, *e.g.*, an enzyme, toxin, hormone, growth factor, drug, etc.; or (b)
20 the variable region, or a portion thereof, is altered, replaced or exchanged with a variable region having a different or altered antigen specificity.

An “anti-T2R” antibody is an antibody or antibody fragment that specifically binds a polypeptide encoded by a T2R gene, cDNA, or a subsequence thereof.

25 The term “immunoassay” is an assay that uses an antibody to specifically bind an antigen. The immunoassay is characterized by the use of specific binding properties of a particular antibody to isolate, target, and/or quantify the antigen.

The phrase “specifically (or selectively) binds” to an antibody or “specifically (or selectively) immunoreactive with,” when referring to a protein or
30 peptide, refers to a binding reaction that is determinative of the presence of the protein in a heterogeneous population of proteins and other biologics. Thus, under designated immunoassay conditions, the specified antibodies bind to a particular protein at least two times the background and do not substantially bind in a significant amount to other proteins present in the sample. Specific binding to an antibody under such conditions

may require an antibody that is selected for its specificity for a particular protein. For example, polyclonal antibodies raised to a T2R family member from specific species such as rat, mouse, or human can be selected to obtain only those polyclonal antibodies that are specifically immunoreactive with the T2R protein or an immunogenic portion thereof and not with other proteins, except for orthologs or polymorphic variants and alleles of the T2R protein. This selection may be achieved by subtracting out antibodies that cross-react with T2R molecules from other species or other T2R molecules. Antibodies can also be selected that recognize only T2R GPCR family members but not GPCRs from other families. A variety of immunoassay formats may be used to select antibodies specifically immunoreactive with a particular protein. For example, solid-phase ELISA immunoassays are routinely used to select antibodies specifically immunoreactive with a protein (see, e.g., Harlow & Lane, *Antibodies, A Laboratory Manual* (1988), for a description of immunoassay formats and conditions that can be used to determine specific immunoreactivity). Typically a specific or selective reaction will be at least twice background signal or noise and more typically more than 10 to 100 times background.

In one embodiment, immunogenic domains corresponding to SEQ ID NOs:166-171 can be used to raise antibodies that specifically bind to polypeptides of the T2R family.

The phrase “selectively associates with” refers to the ability of a nucleic acid to “selectively hybridize” with another as defined above, or the ability of an antibody to “selectively (or specifically) bind to a protein, as defined above.

By “host cell” is meant a cell that contains an expression vector and supports the replication or expression of the expression vector. Host cells may be prokaryotic cells such as *E. coli*, or eukaryotic cells such as yeast, insect, amphibian, or mammalian cells such as CHO, HeLa, HEK-293, and the like, e.g., cultured cells, explants, and cells *in vivo*.

III. Isolation of nucleic acids encoding T2R family members

A. General recombinant DNA methods

This invention relies on routine techniques in the field of recombinant genetics. Basic texts disclosing the general methods of use in this invention include Sambrook *et al.*, *Molecular Cloning, A Laboratory Manual* (2nd ed. 1989); Kriegler,

Gene Transfer and Expression: A Laboratory Manual (1990); and *Current Protocols in Molecular Biology* (Ausubel *et al.*, eds., 1994)).

For nucleic acids, sizes are given in either kilobases (kb) or base pairs (bp). These are estimates derived from agarose or acrylamide gel electrophoresis, from sequenced nucleic acids, or from published DNA sequences. For proteins, sizes are given in kilodaltons (kDa) or amino acid residue numbers. Proteins sizes are estimated from gel electrophoresis, from sequenced proteins, from derived amino acid sequences, or from published protein sequences.

Oligonucleotides that are not commercially available can be chemically synthesized according to the solid phase phosphoramidite triester method first described by Beaucage & Caruthers, *Tetrahedron Letts.* 22:1859-1862 (1981), using an automated synthesizer, as described in Van Devanter *et al.*, *Nucleic Acids Res.* 12:6159-6168 (1984). Purification of oligonucleotides is by either native acrylamide gel electrophoresis or by anion-exchange HPLC as described in Pearson & Reanier, *J. Chrom.* 255:137-149 (1983).

The sequence of the cloned genes and synthetic oligonucleotides can be verified after cloning using, *e.g.*, the chain termination method for sequencing double-stranded templates of Wallace *et al.*, *Gene* 16:21-26 (1981).

B. Cloning methods for the isolation of nucleotide sequences encoding T2R family members

In general, the nucleic acid sequences encoding T2R family members and related nucleic acid sequence homologs are cloned from cDNA and genomic DNA libraries by hybridization with probes, or isolated using amplification techniques with oligonucleotide primers. For example, T2R sequences are typically isolated from mammalian nucleic acid (genomic or cDNA) libraries by hybridizing with a nucleic acid probe, the sequence of which can be derived from SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID

NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, or SEQ ID NO:165. A suitable tissue from which RNA and cDNA for T2R family members can be isolated is tongue tissue, optionally taste bud tissues or individual taste cells.

Amplification techniques using primers can also be used to amplify and isolate T2R sequences from DNA or RNA. For example, degenerate primers encoding the following amino acid sequences can be used to amplify a sequence of a T2R gene: SEQ ID NOS: 166, 167, 168, 169, 170, or 171 (*see, e.g., Dieffenbach & Dveksler, PCR Primer: A Laboratory Manual* (1995)). These primers can be used, *e.g.*, to amplify either the full length sequence or a probe of one to several hundred nucleotides, which is then used to screen a mammalian library for full-length T2R clones. As described above, such primers can be used to isolate a full length sequence, or a probe which can then be used to isolated a full length sequence, *e.g.*, from a library.

Nucleic acids encoding T2R can also be isolated from expression libraries using antibodies as probes. Such polyclonal or monoclonal antibodies can be raised using the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID

NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, or SEQ ID NO:164.

Polymorphic variants, alleles, and interspecies homologs that are substantially identical to a T2R family member can be isolated using T2R nucleic acid probes, and oligonucleotides under stringent hybridization conditions, by screening libraries. Alternatively, expression libraries can be used to clone T2R family members and T2R family member polymorphic variants, alleles, and interspecies homologs, by detecting expressed homologs immunologically with antisera or purified antibodies made against a T2R polypeptide, which also recognize and selectively bind to the T2R homolog.

To make a cDNA library, one should choose a source that is rich in T2R mRNA, *e.g.*, tongue tissue, or isolated taste buds. The mRNA is then made into cDNA using reverse transcriptase, ligated into a recombinant vector, and transfected into a recombinant host for propagation, screening and cloning. Methods for making and screening cDNA libraries are well known (*see, e.g.*, Gubler & Hoffman, *Gene* 25:263-269 (1983); Sambrook *et al.*, *supra*; Ausubel *et al.*, *supra*).

For a genomic library, the DNA is extracted from the tissue and either mechanically sheared or enzymatically digested to yield fragments of about 12-20 kb. The fragments are then separated by gradient centrifugation from undesired sizes and are constructed in bacteriophage lambda vectors. These vectors and phage are packaged *in vitro*. Recombinant phage are analyzed by plaque hybridization as described in Benton & Davis, *Science* 196:180-182 (1977). Colony hybridization is carried out as generally described in Grunstein *et al.*, *Proc. Natl. Acad. Sci. USA.*, 72:3961-3965 (1975).

An alternative method of isolating T2R nucleic acid and its homologs combines the use of synthetic oligonucleotide primers and amplification of an RNA or DNA template (*see* U.S. Patents 4,683,195 and 4,683,202; *PCR Protocols: A Guide to Methods and Applications* (Innis *et al.*, eds, 1990)). Methods such as polymerase chain reaction (PCR) and ligase chain reaction (LCR) can be used to amplify nucleic acid sequences of T2R genes directly from mRNA, from cDNA, from genomic libraries or cDNA libraries. Degenerate oligonucleotides can be designed to amplify T2R family

member homologs using the sequences provided herein. Restriction endonuclease sites can be incorporated into the primers. Polymerase chain reaction or other *in vitro* amplification methods may also be useful, for example, to clone nucleic acid sequences that code for proteins to be expressed, to make nucleic acids to use as probes for detecting the presence of T2R-encoding mRNA in physiological samples, for nucleic acid sequencing, or for other purposes. Genes amplified by the PCR reaction can be purified from agarose gels and cloned into an appropriate vector.

Gene expression of T2R family members can also be analyzed by techniques known in the art, *e.g.*, reverse transcription and amplification of mRNA, isolation of total RNA or poly A⁺ RNA, northern blotting, dot blotting, *in situ* hybridization, RNase protection, probing DNA microchip arrays, and the like. In one embodiment, high density oligonucleotide analysis technology (*e.g.*, GeneChip™) is used to identify homologs and polymorphic variants of the GPCRs of the invention. In the case where the homologs being identified are linked to a known disease, they can be used with GeneChip™ as a diagnostic tool in detecting the disease in a biological sample, *see, e.g.*, Gunthand *et al.*, *AIDS Res. Hum. Retroviruses* 14: 869-876 (1998); Kozal *et al.*, *Nat. Med.* 2:753-759 (1996); Matson *et al.*, *Anal. Biochem.* 224:110-106 (1995); Lockhart *et al.*, *Nat. Biotechnol.* 14:1675-1680 (1996); Gingeras *et al.*, *Genome Res.* 8:435-448 (1998); Hacia *et al.*, *Nucleic Acids Res.* 26:3865-3866 (1998).

Synthetic oligonucleotides can be used to construct recombinant T2R genes for use as probes or for expression of protein. This method is performed using a series of overlapping oligonucleotides usually 40- 120 bp in length, representing both the sense and nonsense strands of the gene. These DNA fragments are then annealed, ligated and cloned. Alternatively, amplification techniques can be used with precise primers to amplify a specific subsequence of the T2R nucleic acid. The specific subsequence is then ligated into an expression vector.

The nucleic acid encoding a T2R gene is typically cloned into intermediate vectors before transformation into prokaryotic or eukaryotic cells for replication and/or expression. These intermediate vectors are typically prokaryote vectors, *e.g.*, plasmids, or shuttle vectors.

Optionally, nucleic acids encoding chimeric proteins comprising a T2R polypeptide or domains thereof can be made according to standard techniques. For example, a domain such as a ligand binding domain (*e.g.*, an extracellular domain alone,

an extracellular domain plus a transmembrane region, or a transmembrane region alone), an extracellular domain, a transmembrane domain (*e.g.*, one comprising up to seven transmembrane regions and corresponding extracellular and cytosolic loops), the transmembrane domain and a cytoplasmic domain, an active site, a subunit association region, *etc.*, can be covalently linked to a heterologous protein. For example, an extracellular domain can be linked to a heterologous GPCR transmembrane domain, or a heterologous GPCR extracellular domain can be linked to a transmembrane domain. Other heterologous proteins of choice include, *e.g.*, green fluorescent protein, β -gal, glutamate receptor, and the rhodopsin presequence.

C. *Expression in prokaryotes and eukaryotes*

To obtain high level expression of a cloned gene or nucleic acid, such as those cDNAs encoding a T2R family member, one typically subclones the T2R sequence into an expression vector that contains a strong promoter to direct transcription, a transcription/translation terminator, and if for a nucleic acid encoding a protein, a ribosome binding site for translational initiation. Suitable bacterial promoters are well known in the art and described, *e.g.*, in Sambrook *et al.* and Ausubel *et al.* Bacterial expression systems for expressing the T2R protein are available in, *e.g.*, *E. coli*, *Bacillus sp.*, and *Salmonella* (Palva *et al.*, *Gene* 22:229-235 (1983); Mosbach *et al.*, *Nature* 302:543-545 (1983). Kits for such expression systems are commercially available. Eukaryotic expression systems for mammalian cells, yeast, and insect cells are well known in the art and are also commercially available. In one embodiment, the eukaryotic expression vector is an adenoviral vector, an adeno-associated vector, or a retroviral vector.

The promoter used to direct expression of a heterologous nucleic acid depends on the particular application. The promoter is optionally positioned about the same distance from the heterologous transcription start site as it is from the transcription start site in its natural setting. As is known in the art, however, some variation in this distance can be accommodated without loss of promoter function.

In addition to the promoter, the expression vector typically contains a transcription unit or expression cassette that contains all the additional elements required for the expression of the T2R-encoding nucleic acid in host cells. A typical expression cassette thus contains a promoter operably linked to the nucleic acid sequence encoding a

T2R and signals required for efficient polyadenylation of the transcript, ribosome binding sites, and translation termination. The nucleic acid sequence encoding a T2R may typically be linked to a cleavable signal peptide sequence to promote secretion of the encoded protein by the transformed cell. Such signal peptides would include, among
5 others, the signal peptides from tissue plasminogen activator, insulin, and neuron growth factor, and juvenile hormone esterase of *Heliothis virescens*. Additional elements of the cassette may include enhancers and, if genomic DNA is used as the structural gene, introns with functional splice donor and acceptor sites.

In addition to a promoter sequence, the expression cassette should also
10 contain a transcription termination region downstream of the structural gene to provide for efficient termination. The termination region may be obtained from the same gene as the promoter sequence or may be obtained from different genes.

The particular expression vector used to transport the genetic information into the cell is not particularly critical. Any of the conventional vectors used for
15 expression in eukaryotic or prokaryotic cells may be used. Standard bacterial expression vectors include plasmids such as pBR322 based plasmids, pSKF, pET23D, and fusion expression systems such as GST and LacZ. Epitope tags can also be added to recombinant proteins to provide convenient methods of isolation, *e.g.*, c-myc.

Expression vectors containing regulatory elements from eukaryotic viruses
20 are typically used in eukaryotic expression vectors, *e.g.*, SV40 vectors, papilloma virus vectors, and vectors derived from Epstein-Barr virus. Other exemplary eukaryotic vectors include pMSG, pAV009/A⁺, pMTO10/A⁺, pMAMneo-5, baculovirus pDSVE, and any other vector allowing expression of proteins under the direction of the SV40 early promoter, SV40 later promoter, metallothionein promoter, murine mammary tumor
25 virus promoter, Rous sarcoma virus promoter, polyhedrin promoter, or other promoters shown effective for expression in eukaryotic cells.

Some expression systems have markers that provide gene amplification such as neomycin, hymidine kinase, hygromycin B phosphotransferase, and dihydrofolate reductase. Alternatively, high yield expression systems not involving gene amplification
30 are also suitable, such as using a baculovirus vector in insect cells, with a sequence encoding a T2R family member under the direction of the polyhedrin promoter or other strong baculovirus promoters.

The elements that are typically included in expression vectors also include a replicon that functions in *E. coli*, a gene encoding antibiotic resistance to permit

selection of bacteria that harbor recombinant plasmids, and unique restriction sites in nonessential regions of the plasmid to allow insertion of eukaryotic sequences. The particular antibiotic resistance gene chosen is not critical, any of the many resistance genes known in the art are suitable. The prokaryotic sequences are optionally chosen such that they do not interfere with the replication of the DNA in eukaryotic cells, if necessary.

Standard transfection methods are used to produce bacterial, mammalian, yeast or insect cell lines that express large quantities of a T2R protein, which are then purified using standard techniques (*see, e.g., Colley et al., J. Biol. Chem.* 264:17619-17622 (1989); *Guide to Protein Purification*, in *Methods in Enzymology*, vol. 182 (Deutscher, ed., 1990)). Transformation of eukaryotic and prokaryotic cells are performed according to standard techniques (*see, e.g., Morrison, J. Bact.* 132:349-351 (1977); Clark-Curtiss & Curtiss, *Methods in Enzymology* 101:347-362 (Wu *et al.*, eds, 1983).

Any of the well known procedures for introducing foreign nucleotide sequences into host cells may be used. These include the use of calcium phosphate transfection, polybrene, protoplast fusion, electroporation, liposomes, microinjection, plasma vectors, viral vectors and any of the other well known methods for introducing cloned genomic DNA, cDNA, synthetic DNA or other foreign genetic material into a host cell (*see, e.g., Sambrook et al., supra*). It is only necessary that the particular genetic engineering procedure used be capable of successfully introducing at least one gene into the host cell capable of expressing a T2R gene.

In one preferred embodiment, a polynucleotide encoding a T2R is operably linked to a EF-1 α promoter, *e.g.*, using a pEAK10 mammalian expression vector (Edge Biosystems, MD) is used. Such vectors can be introduced into cells, *e.g.*, HEK-293 cells using any standard method, such as transfection using LipofectAMINE (Lifetechnologies).

After the expression vector is introduced into the cells, the transfected cells are cultured under conditions favoring expression of the T2R family member, which is recovered from the culture using standard techniques identified below.

IV. Purification of T2R polypeptides

Either naturally occurring or recombinant T2R polypeptides can be purified for use in functional assays. Optionally, recombinant T2R polypeptides are purified. Naturally occurring T2R polypeptides are purified, *e.g.*, from mammalian tissue
5 such as tongue tissue, and any other source of a T2R homolog. Recombinant T2R polypeptides are purified from any suitable bacterial or eukaryotic expression system, *e.g.*, CHO cells or insect cells.

T2R proteins may be purified to substantial purity by standard techniques, including selective precipitation with such substances as ammonium sulfate; column
10 chromatography, immunopurification methods, and others (*see, e.g.*, Scopes, *Protein Purification: Principles and Practice* (1982); U.S. Patent No. 4,673,641; Ausubel *et al.*, *supra*; and Sambrook *et al.*, *supra*).

A number of procedures can be employed when recombinant T2R family members are being purified. For example, proteins having established molecular
15 adhesion properties can be reversibly fused to the T2R polypeptide. With the appropriate ligand, a T2R can be selectively adsorbed to a purification column and then freed from the column in a relatively pure form. The fused protein is then removed by enzymatic activity. Finally T2R proteins can be purified using immunoaffinity columns.

20 A. Purification of T2R protein from recombinant cells

Recombinant proteins are expressed by transformed bacteria or eukaryotic cells such as CHO cells or insect cells in large amounts, typically after promoter induction; but expression can be constitutive. Promoter induction with IPTG is a one
25 example of an inducible promoter system. Cells are grown according to standard procedures in the art. Fresh or frozen cells are used for isolation of protein.

Proteins expressed in bacteria may form insoluble aggregates ("inclusion bodies"). Several protocols are suitable for purification of T2R inclusion bodies. For example, purification of inclusion bodies typically involves the extraction, separation and/or purification of inclusion bodies by disruption of bacterial cells, *e.g.*, by incubation
30 in a buffer of 50 mM TRIS/HCL pH 7.5, 50 mM NaCl, 5 mM MgCl₂, 1 mM DTT, 0.1 mM ATP, and 1 mM PMSF. The cell suspension can be lysed using 2-3 passages through a French Press, homogenized using a Polytron (Brinkman Instruments) or sonicated on ice. Alternate methods of lysing bacteria are apparent to those of skill in the art (*see, e.g.*, Sambrook *et al.*, *supra*; Ausubel *et al.*, *supra*).

If necessary, the inclusion bodies are solubilized, and the lysed cell suspension is typically centrifuged to remove unwanted insoluble matter. Proteins that formed the inclusion bodies may be renatured by dilution or dialysis with a compatible buffer. Suitable solvents include, but are not limited to urea (from about 4 M to about 8 M), formamide (at least about 80%, volume/volume basis), and guanidine hydrochloride (from about 4 M to about 8 M). Some solvents which are capable of solubilizing aggregate-forming proteins, for example SDS (sodium dodecyl sulfate), 70% formic acid, are inappropriate for use in this procedure due to the possibility of irreversible denaturation of the proteins, accompanied by a lack of immunogenicity and/or activity. Although guanidine hydrochloride and similar agents are denaturants, this denaturation is not irreversible and renaturation may occur upon removal (by dialysis, for example) or dilution of the denaturant, allowing re-formation of immunologically and/or biologically active protein. Other suitable buffers are known to those skilled in the art. T2R polypeptides are separated from other bacterial proteins by standard separation techniques, *e.g.*, with Ni-NTA agarose resin.

Alternatively, it is possible to purify T2R polypeptides from bacteria periplasm. After lysis of the bacteria, when a T2R protein is exported into the periplasm of the bacteria, the periplasmic fraction of the bacteria can be isolated by cold osmotic shock in addition to other methods known to skill in the art. To isolate recombinant proteins from the periplasm, the bacterial cells are centrifuged to form a pellet. The pellet is resuspended in a buffer containing 20% sucrose. To lyse the cells, the bacteria are centrifuged and the pellet is resuspended in ice-cold 5 mM MgSO₄ and kept in an ice bath for approximately 10 minutes. The cell suspension is centrifuged and the supernatant decanted and saved. The recombinant proteins present in the supernatant can be separated from the host proteins by standard separation techniques well known to those of skill in the art.

B. Standard protein separation techniques for purifying T2R polypeptides

Solubility fractionation

Often as an initial step, particularly if the protein mixture is complex, an initial salt fractionation can separate many of the unwanted host cell proteins (or proteins derived from the cell culture media) from the recombinant protein of interest. The preferred salt is ammonium sulfate. Ammonium sulfate precipitates proteins by effectively reducing the amount of water in the protein mixture. Proteins then precipitate

on the basis of their solubility. The more hydrophobic a protein is, the more likely it is to precipitate at lower ammonium sulfate concentrations. A typical protocol includes adding saturated ammonium sulfate to a protein solution so that the resultant ammonium sulfate concentration is between 20-30%. This concentration will precipitate the most hydrophobic of proteins. The precipitate is then discarded (unless the protein of interest is hydrophobic) and ammonium sulfate is added to the supernatant to a concentration known to precipitate the protein of interest. The precipitate is then solubilized in buffer and the excess salt removed if necessary, either through dialysis or diafiltration. Other methods that rely on solubility of proteins, such as cold ethanol precipitation, are well known to those of skill in the art and can be used to fractionate complex protein mixtures.

Size differential filtration

The molecular weight of a T2R protein can be used to isolate it from proteins of greater and lesser size using ultrafiltration through membranes of different pore size (for example, Amicon or Millipore membranes). As a first step, the protein mixture is ultrafiltered through a membrane with a pore size that has a lower molecular weight cut-off than the molecular weight of the protein of interest. The retentate of the ultrafiltration is then ultrafiltered against a membrane with a molecular cut off greater than the molecular weight of the protein of interest. The recombinant protein will pass through the membrane into the filtrate. The filtrate can then be chromatographed as described below.

Column chromatography

T2R proteins can also be separated from other proteins on the basis of its size, net surface charge, hydrophobicity, and affinity for ligands. In addition, antibodies raised against proteins can be conjugated to column matrices and the proteins immunopurified. All of these methods are well known in the art. It will be apparent to one of skill that chromatographic techniques can be performed at any scale and using equipment from many different manufacturers (*e.g.*, Pharmacia Biotech).

30

V. Immunological detection of T2R polypeptides

In addition to the detection of T2R genes and gene expression using nucleic acid hybridization technology, one can also use immunoassays to detect T2R, *e.g.*, to identify taste receptor cells, especially bitter taste receptor cells, and variants of

T2R family members. Immunoassays can be used to qualitatively or quantitatively analyze the T2R. A general overview of the applicable technology can be found in Harlow & Lane, *Antibodies: A Laboratory Manual* (1988).

5 A. *Antibodies to T2R family members*

Methods of producing polyclonal and monoclonal antibodies that react specifically with a T2R family member are known to those of skill in the art (*see, e.g.,* Coligan, *Current Protocols in Immunology* (1991); Harlow & Lane, *supra*; Goding, *Monoclonal Antibodies: Principles and Practice* (2d ed. 1986); and Kohler & Milstein, *Nature* 256:495-497 (1975)). Such techniques include antibody preparation by selection of antibodies from libraries of recombinant antibodies in phage or similar vectors, as well as preparation of polyclonal and monoclonal antibodies by immunizing rabbits or mice (*see, e.g.,* Huse *et al.*, *Science* 246:1275-1281 (1989); Ward *et al.*, *Nature* 341:544-546 (1989)).

15 A number of T2R-comprising immunogens may be used to produce antibodies specifically reactive with a T2R family member. For example, a recombinant T2R protein, or an antigenic fragment thereof, is isolated as described herein. Suitable antigenic regions include, *e.g.,* the conserved motifs that are used to identify members of the T2R family, *i.e.,* SEQ ID NOS:166, 167, 168, 169, 170, and 171. Recombinant
20 protein can be expressed in eukaryotic or prokaryotic cells as described above, and purified as generally described above. Recombinant protein is the preferred immunogen for the production of monoclonal or polyclonal antibodies. Alternatively, a synthetic peptide derived from the sequences disclosed herein and conjugated to a carrier protein can be used an immunogen. Naturally occurring protein may also be used either in pure
25 or impure form. The product is then injected into an animal capable of producing antibodies. Either monoclonal or polyclonal antibodies may be generated, for subsequent use in immunoassays to measure the protein.

Methods of production of polyclonal antibodies are known to those of skill in the art. An inbred strain of mice (*e.g.,* BALB/C mice) or rabbits is immunized with the
30 protein using a standard adjuvant, such as Freund's adjuvant, and a standard immunization protocol. The animal's immune response to the immunogen preparation is monitored by taking test bleeds and determining the titer of reactivity to the T2R. When appropriately high titers of antibody to the immunogen are obtained, blood is collected

from the animal and antisera are prepared. Further fractionation of the antisera to enrich for antibodies reactive to the protein can be done if desired (*see* Harlow & Lane, *supra*).

Monoclonal antibodies may be obtained by various techniques familiar to those skilled in the art. Briefly, spleen cells from an animal immunized with a desired antigen are immortalized, commonly by fusion with a myeloma cell (*see* Kohler & Milstein, *Eur. J. Immunol.* 6:511-519 (1976)). Alternative methods of immortalization include transformation with Epstein Barr Virus, oncogenes, or retroviruses, or other methods well known in the art. Colonies arising from single immortalized cells are screened for production of antibodies of the desired specificity and affinity for the antigen, and yield of the monoclonal antibodies produced by such cells may be enhanced by various techniques, including injection into the peritoneal cavity of a vertebrate host. Alternatively, one may isolate DNA sequences which encode a monoclonal antibody or a binding fragment thereof by screening a DNA library from human B cells according to the general protocol outlined by Huse *et al.*, *Science* 246:1275-1281 (1989).

Monoclonal antibodies and polyclonal sera are collected and titrated against the immunogen protein in an immunoassay, for example, a solid phase immunoassay with the immunogen immobilized on a solid support. Typically, polyclonal antisera with a titer of 10^4 or greater are selected and tested for their cross reactivity against non-T2R proteins, or even other T2R family members or other related proteins from other organisms, using a competitive binding immunoassay. Specific polyclonal antisera and monoclonal antibodies will usually bind with a K_d of at least about 0.1 mM, more usually at least about 1 μ M, optionally at least about 0.1 μ M or better, and optionally 0.01 μ M or better.

Once T2R family member specific antibodies are available, individual T2R proteins can be detected by a variety of immunoassay methods. For a review of immunological and immunoassay procedures, see *Basic and Clinical Immunology* (Stites & Terr eds., 7th ed. 1991). Moreover, the immunoassays of the present invention can be performed in any of several configurations, which are reviewed extensively in *Enzyme Immunoassay* (Maggio, ed., 1980); and Harlow & Lane, *supra*.

B. Immunological binding assays

T2R proteins can be detected and/or quantified using any of a number of well recognized immunological binding assays (*see, e.g.*, U.S. Patents 4,366,241; 4,376,110; 4,517,288; and 4,837,168). For a review of the general immunoassays, see

also *Methods in Cell Biology: Antibodies in Cell Biology*, volume 37 (Asai, ed. 1993); *Basic and Clinical Immunology* (Stites & Terr, eds., 7th ed. 1991). Immunological binding assays (or immunoassays) typically use an antibody that specifically binds to a protein or antigen of choice (in this case a T2R family member or an antigenic subsequence thereof). The antibody (*e.g.*, anti-T2R) may be produced by any of a number of means well known to those of skill in the art and as described above.

Immunoassays also often use a labeling agent to specifically bind to and label the complex formed by the antibody and antigen. The labeling agent may itself be one of the moieties comprising the antibody/antigen complex. Thus, the labeling agent may be a labeled T2R polypeptide or a labeled anti-T2R antibody. Alternatively, the labeling agent may be a third moiety, such a secondary antibody, that specifically binds to the antibody/T2R complex (a secondary antibody is typically specific to antibodies of the species from which the first antibody is derived). Other proteins capable of specifically binding immunoglobulin constant regions, such as protein A or protein G may also be used as the label agent. These proteins exhibit a strong non-immunogenic reactivity with immunoglobulin constant regions from a variety of species (*see, e.g.*, Kronval *et al.*, *J. Immunol.* 111:1401-1406 (1973); Akerstrom *et al.*, *J. Immunol.* 135:2589-2542 (1985)). The labeling agent can be modified with a detectable moiety, such as biotin, to which another molecule can specifically bind, such as streptavidin. A variety of detectable moieties are well known to those skilled in the art.

Throughout the assays, incubation and/or washing steps may be required after each combination of reagents. Incubation steps can vary from about 5 seconds to several hours, optionally from about 5 minutes to about 24 hours. However, the incubation time will depend upon the assay format, antigen, volume of solution, concentrations, and the like. Usually, the assays will be carried out at ambient temperature, although they can be conducted over a range of temperatures, such as 10°C to 40°C.

Non-competitive assay formats

Immunoassays for detecting a T2R protein in a sample may be either competitive or noncompetitive. Noncompetitive immunoassays are assays in which the amount of antigen is directly measured. In one preferred “sandwich” assay, for example, the anti-T2R antibodies can be bound directly to a solid substrate on which they are

immobilized. These immobilized antibodies then capture the T2R protein present in the test sample. The T2R protein is thus immobilized is then bound by a labeling agent, such as a second T2R antibody bearing a label. Alternatively, the second antibody may lack a label, but it may, in turn, be bound by a labeled third antibody specific to antibodies of the species from which the second antibody is derived. The second or third antibody is typically modified with a detectable moiety, such as biotin, to which another molecule specifically binds, *e.g.*, streptavidin, to provide a detectable moiety.

Competitive assay formats

In competitive assays, the amount of T2R protein present in the sample is measured indirectly by measuring the amount of a known, added (exogenous) T2R protein displaced (competed away) from an anti-T2R antibody by the unknown T2R protein present in a sample. In one competitive assay, a known amount of T2R protein is added to a sample and the sample is then contacted with an antibody that specifically binds to the T2R. The amount of exogenous T2R protein bound to the antibody is inversely proportional to the concentration of T2R protein present in the sample. In a particularly preferred embodiment, the antibody is immobilized on a solid substrate. The amount of T2R protein bound to the antibody may be determined either by measuring the amount of T2R protein present in a T2R/antibody complex, or alternatively by measuring the amount of remaining uncomplexed protein. The amount of T2R protein may be detected by providing a labeled T2R molecule.

A hapten inhibition assay is another preferred competitive assay. In this assay the known T2R protein is immobilized on a solid substrate. A known amount of anti-T2R antibody is added to the sample, and the sample is then contacted with the immobilized T2R. The amount of anti-T2R antibody bound to the known immobilized T2R protein is inversely proportional to the amount of T2R protein present in the sample. Again, the amount of immobilized antibody may be detected by detecting either the immobilized fraction of antibody or the fraction of the antibody that remains in solution. Detection may be direct where the antibody is labeled or indirect by the subsequent addition of a labeled moiety that specifically binds to the antibody as described above.

Cross-reactivity determinations

Immunoassays in the competitive binding format can also be used for crossreactivity determinations. For example, a protein at least partially encoded by SEQ

ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12,
 SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ
 ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID
 NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID
 5 NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, SEQ ID NO:63, SEQ ID
 NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID
 NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID
 NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID NO:106, SEQ ID
 NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID
 10 NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID NO:124, SEQ ID
 NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID
 NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID
 NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID
 NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, or SEQ
 15 ID NO:165, can be immobilized to a solid support. Proteins (*e.g.*, T2R proteins and
 homologs) are added to the assay that compete for binding of the antisera to the
 immobilized antigen. The ability of the added proteins to compete for binding of the
 antisera to the immobilized protein is compared to the ability of the T2R polypeptide
 encoded by SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10,
 20 SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ
 ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID
 NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID
 NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, SEQ ID
 NO:63, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID
 25 NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID
 NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID
 NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID
 NO:116, SEQ ID NO:118, SEQ ID NO:120, SEQ ID NO:120, SEQ ID NO:122, SEQ ID
 NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID
 30 NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID
 NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID
 NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID
 NO:163, or SEQ ID NO:165 to compete with itself. The percent crossreactivity for the
 above proteins is calculated, using standard calculations. Those antisera with less than

10% crossreactivity with each of the added proteins listed above are selected and pooled. The cross-reacting antibodies are optionally removed from the pooled antisera by immunoabsorption with the added considered proteins, *e.g.*, distantly related homologs. In addition, peptides comprising amino acid sequences representing conserved motifs that are used to identify members of the T2R family can be used in cross-reactivity determinations, *i.e.*, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168; SEQ ID NO:169, SEQ ID NO:170, or SEQ ID NO:171.

The immunoabsorbed and pooled antisera are then used in a competitive binding immunoassay as described above to compare a second protein, thought to be perhaps an allele or polymorphic variant of a T2R family member, to the immunogen protein (*i.e.*, T2R protein encoded by SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, SEQ ID NO:63, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, ~~SEQ ID NO:120~~, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, or SEQ ID NO:165). In order to make this comparison, the two proteins are each assayed at a wide range of concentrations and the amount of each protein required to inhibit 50% of the binding of the antisera to the immobilized protein is determined. If the amount of the second protein required to inhibit 50% of binding is less than 10 times the amount of the protein encoded by SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:57, SEQ ID NO:61, SEQ ID NO:63, SEQ ID

NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86; SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:104 SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:114, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120, ~~SEQ ID NO:120~~, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:128, SEQ ID NO:130, SEQ ID NO:132, SEQ ID NO:134, SEQ ID NO:136, SEQ ID NO:138, SEQ ID NO:140, SEQ ID NO:142, SEQ ID NO:144, SEQ ID NO:146, SEQ ID NO:148, SEQ ID NO:150, SEQ ID NO:152, SEQ ID NO:154, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:159, SEQ ID NO:161, SEQ ID NO:163, or SEQ ID NO:165 that is required to inhibit 50% of binding, then the second protein is said to specifically bind to the polyclonal antibodies generated to a T2R immunogen.

Antibodies raised against SEQ ID NOs:166-171 can also be used to prepare antibodies that specifically bind only to GPCRs of the T2R family, but not to GPCRs from other families.

Polyclonal antibodies that specifically bind to a particular member of the T2R family, *e.g.*, T2R01, can be made by subtracting out cross-reactive antibodies using other T2R family members. Species-specific polyclonal antibodies can be made in a similar way. For example, antibodies specific to human T2R01 can be made by subtracting out antibodies that are cross-reactive with orthologous sequences, *e.g.*, rat T2R01 or mouse T2R19.

Other assay formats

Western blot (immunoblot) analysis is used to detect and quantify the presence of T2R protein in the sample. The technique generally comprises separating sample proteins by gel electrophoresis on the basis of molecular weight, transferring the separated proteins to a suitable solid support, (such as a nitrocellulose filter, a nylon filter, or derivatized nylon filter), and incubating the sample with the antibodies that specifically bind the T2R protein. The anti-T2R polypeptide antibodies specifically bind to the T2R polypeptide on the solid support. These antibodies may be directly labeled or alternatively may be subsequently detected using labeled antibodies (*e.g.*, labeled sheep anti-mouse antibodies) that specifically bind to the anti-T2R antibodies.

Other assay formats include liposome immunoassays (LIA), which use liposomes designed to bind specific molecules (*e.g.*, antibodies) and release encapsulated

reagents or markers. The released chemicals are then detected according to standard techniques (see Monroe *et al.*, *Amer. Clin. Prod. Rev.* 5:34-41 (1986)).

Reduction of non-specific binding

5 One of skill in the art will appreciate that it is often desirable to minimize non-specific binding in immunoassays. Particularly, where the assay involves an antigen or antibody immobilized on a solid substrate it is desirable to minimize the amount of non-specific binding to the substrate. Means of reducing such non-specific binding are well known to those of skill in the art. Typically, this technique involves coating the
10 substrate with a proteinaceous composition. In particular, protein compositions such as bovine serum albumin (BSA), nonfat powdered milk, and gelatin are widely used with powdered milk being most preferred.

Labels

15 The particular label or detectable group used in the assay is not a critical aspect of the invention, as long as it does not significantly interfere with the specific binding of the antibody used in the assay. The detectable group can be any material having a detectable physical or chemical property. Such detectable labels have been well-developed in the field of immunoassays and, in general, most any label useful in such
20 methods can be applied to the present invention. Thus, a label is any composition detectable by spectroscopic, photochemical, biochemical, immunochemical, electrical, optical or chemical means. Useful labels in the present invention include magnetic beads (*e.g.*, DYNABEADS™), fluorescent dyes (*e.g.*, fluorescein isothiocyanate, Texas red, rhodamine, and the like), radiolabels (*e.g.*, ³H, ¹²⁵I, ³⁵S, ¹⁴C, or ³²P), enzymes (*e.g.*, horse
25 radish peroxidase, alkaline phosphatase and others commonly used in an ELISA), and colorimetric labels such as colloidal gold or colored glass or plastic beads (*e.g.*, polystyrene, polypropylene, latex, *etc.*).

 The label may be coupled directly or indirectly to the desired component of the assay according to methods well known in the art. As indicated above, a wide
30 variety of labels may be used, with the choice of label depending on sensitivity required, ease of conjugation with the compound, stability requirements, available instrumentation, and disposal provisions.

 Non-radioactive labels are often attached by indirect means. Generally, a ligand molecule (*e.g.*, biotin) is covalently bound to the molecule. The ligand then binds

to another molecules (*e.g.*, streptavidin) molecule, which is either inherently detectable or covalently bound to a signal system, such as a detectable enzyme, a fluorescent compound, or a chemiluminescent compound. The ligands and their targets can be used in any suitable combination with antibodies that recognize a T2R protein, or secondary
5 antibodies that recognize anti-T2R.

The molecules can also be conjugated directly to signal generating compounds, *e.g.*, by conjugation with an enzyme or fluorophore. Enzymes of interest as labels will primarily be hydrolases, particularly phosphatases, esterases and glycosidases, or oxidotases, particularly peroxidases. Fluorescent compounds include fluorescein and
10 its derivatives, rhodamine and its derivatives, dansyl, umbelliferone, *etc.* Chemiluminescent compounds include luciferin, and 2,3-dihydrophthalazinediones, *e.g.*, luminol. For a review of various labeling or signal producing systems that may be used, see U.S. Patent No. 4,391,904.

Means of detecting labels are well known to those of skill in the art. Thus,
15 for example, where the label is a radioactive label, means for detection include a scintillation counter or photographic film as in autoradiography. Where the label is a fluorescent label, it may be detected by exciting the fluorochrome with the appropriate wavelength of light and detecting the resulting fluorescence. The fluorescence may be detected visually, by means of photographic film, by the use of electronic detectors such
20 as charge coupled devices (CCDs) or photomultipliers and the like. Similarly, enzymatic labels may be detected by providing the appropriate substrates for the enzyme and detecting the resulting reaction product. Finally simple colorimetric labels may be detected simply by observing the color associated with the label. Thus, in various dipstick assays, conjugated gold often appears pink, while various conjugated beads
25 appear the color of the bead.

Some assay formats do not require the use of labeled components. For instance, agglutination assays can be used to detect the presence of the target antibodies. In this case, antigen-coated particles are agglutinated by samples comprising the target antibodies. In this format, none of the components need be labeled and the presence of
30 the target antibody is detected by simple visual inspection.

VI. Assays for modulators of T2R family members

A. Assays for T2R protein activity

T2R family members and their alleles and polymorphic variants are G-protein coupled receptors that participate in taste transduction, *e.g.*, bitter taste

5 transduction. The activity of T2R polypeptides can be assessed using a variety of *in vitro* and *in vivo* assays to determine functional, chemical, and physical effects, *e.g.*, measuring ligand binding (*e.g.*, radioactive ligand binding), second messengers (*e.g.*, cAMP, cGMP, IP₃, DAG, or Ca²⁺), ion flux, phosphorylation levels, transcription levels, neurotransmitter levels, and the like. Furthermore, such assays can be used to test for inhibitors and
10 activators of T2R family members. Modulators can also be genetically altered versions of T2R receptors. Such modulators of taste transduction activity are useful for customizing taste, for example to modify the detection of bitter tastes.

The T2R protein of the assay will typically be selected from a polypeptide having a sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ
15 ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID
20 NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID
25 NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID
30 NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, or SEQ ID NO:164 or conservatively modified variant thereof.

Alternatively, the T2R protein of the assay will be derived from a eukaryote and include an amino acid subsequence having amino acid sequence identity to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5; SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:97, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:103, SEQ ID NO:105, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:111, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:123, SEQ ID NO:125, SEQ ID NO:127, SEQ ID NO:129, SEQ ID NO:131, SEQ ID NO:133, SEQ ID NO:135, SEQ ID NO:137, SEQ ID NO:139, SEQ ID NO:141, SEQ ID NO:143, SEQ ID NO:145, SEQ ID NO:147, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:153, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:162, or SEQ ID NO:164. Generally, the amino acid sequence identity will be at least 60%, optionally at least 70% to 85%, optionally at least 90-95%. Optionally, the polypeptide of the assays will comprise a domain of a T2R protein, such as an extracellular domain, transmembrane region, transmembrane domain, cytoplasmic domain, ligand binding domain, subunit association domain, active site, and the like. Either the T2R protein or a domain thereof can be covalently linked to a heterologous protein to create a chimeric protein used in the assays described herein.

Modulators of T2R receptor activity are tested using T2R polypeptides as described above, either recombinant or naturally occurring. The protein can be isolated, expressed in a cell, expressed in a membrane derived from a cell, expressed in tissue or in an animal, either recombinant or naturally occurring. For example, tongue slices, dissociated cells from a tongue, transformed cells, or membranes can be used. Modulation is tested using one of the *in vitro* or *in vivo* assays described herein. Taste transduction can also be examined *in vitro* with soluble or solid state reactions, using a full-length

T2R-GPCR or a chimeric molecule such as an extracellular domain or transmembrane region, or combination thereof, of a T2R receptor covalently linked to a heterologous signal transduction domain, or a heterologous extracellular domain and/or transmembrane region covalently linked to the transmembrane and/or cytoplasmic domain of a T2R receptor. Furthermore, ligand-binding domains of the protein of interest can be used *in vitro* in soluble or solid state reactions to assay for ligand binding. In numerous embodiments, a chimeric receptor will be made that comprises all or part of a T2R polypeptide as well an additional sequence that facilitates the localization of the T2R to the membrane, such as a rhodopsin, *e.g.*, an N-terminal fragment of a rhodopsin protein.

Ligand binding to a T2R protein, a domain, or chimeric protein can be tested in solution, in a bilayer membrane, attached to a solid phase, in a lipid monolayer, or in vesicles. Binding of a modulator can be tested using, *e.g.*, changes in spectroscopic characteristics (*e.g.*, fluorescence, absorbance, refractive index) hydrodynamic (*e.g.*, shape), chromatographic, or solubility properties.

Receptor-G-protein interactions can also be examined. For example, binding of the G-protein to the receptor or its release from the receptor can be examined. For example, in the absence of GTP, an activator will lead to the formation of a tight complex of a G protein (all three subunits) with the receptor. This complex can be detected in a variety of ways, as noted above. Such an assay can be modified to search for inhibitors, *e.g.*, by adding an activator to the receptor and G protein in the absence of GTP, which form a tight complex, and then screen for inhibitors by looking at dissociation of the receptor-G protein complex. In the presence of GTP, release of the alpha subunit of the G protein from the other two G protein subunits serves as a criterion of activation.

In particularly preferred embodiments, T2R-Gustducin interactions are monitored as a function of T2R receptor activation. As shown in Example IX, mouse T2R5 shows strong cycloheximide-dependent coupling with Gustducin. Such ligand dependent coupling of T2R receptors with Gustducin can be used as a marker to identify modifiers of any member of the T2R family.

An activated or inhibited G-protein will in turn alter the properties of target enzymes, channels, and other effector proteins. The classic examples are the activation of cGMP phosphodiesterase by transducin in the visual system, adenylate cyclase by the stimulatory G-protein, phospholipase C by Gq and other cognate G proteins, and modulation of diverse channels by Gi and other G proteins. Downstream

consequences can also be examined such as generation of diacyl glycerol and IP3 by phospholipase C, and in turn, for calcium mobilization by IP3.

In a preferred embodiment, a T2R polypeptide is expressed in a eukaryotic cell as a chimeric receptor with a heterologous, chaperone sequence that facilitates its maturation and targeting through the secretory pathway. In a preferred embodiment, the heterologous sequence is a rhodopsin sequence, such as an N-terminal fragment of a rhodopsin. Such chimeric T2R receptors can be expressed in any eukaryotic cell, such as HEK-293 cells. Preferably, the cells comprise a functional G protein, *e.g.*, G α 15, that is capable of coupling the chimeric receptor to an intracellular signaling pathway or to a signaling protein such as phospholipase C β . Activation of such chimeric receptors in such cells can be detected using any standard method, such as by detecting changes in intracellular calcium by detecting FURA-2 dependent fluorescence in the cell.

Activated GPCR receptors become substrates for kinases that phosphorylate the C-terminal tail of the receptor (and possibly other sites as well). Thus, activators will promote the transfer of ^{32}P from gamma-labeled GTP to the receptor, which can be assayed with a scintillation counter. The phosphorylation of the C-terminal tail will promote the binding of arrestin-like proteins and will interfere with the binding of G-proteins. The kinase/arrestin pathway plays a key role in the desensitization of many GPCR receptors. For example, compounds that modulate the duration a taste receptor stays active would be useful as a means of prolonging a desired taste or cutting off an unpleasant one. For a general review of GPCR signal transduction and methods of assaying signal transduction, *see, e.g., Methods in Enzymology*, vols. 237 and 238 (1994) and volume 96 (1983); Bourne *et al.*, *Nature* 10:349:117-27 (1991); Bourne *et al.*, *Nature* 348:125-32 (1990); Pitcher *et al.*, *Annu. Rev. Biochem.* 67:653-92 (1998).

Samples or assays that are treated with a potential T2R protein inhibitor or activator are compared to control samples without the test compound, to examine the extent of modulation. Such assays may be carried out in the presence of a bitter tastant that is known to activate the particular receptor, and modulation of the bitter-tastant-dependent activation monitored. Control samples (untreated with activators or inhibitors) are assigned a relative T2R activity value of 100. Inhibition of a T2R protein is achieved when the T2R activity value relative to the control is about 90%, optionally 50%, optionally 25-0%. Activation of a T2R protein is achieved when the T2R activity value relative to the control is 110%, optionally 150%, 200-500%, or 1000-2000%.

Changes in ion flux may be assessed by determining changes in polarization (*i.e.*, electrical potential) of the cell or membrane expressing a T2R protein. One means to determine changes in cellular polarization is by measuring changes in current (thereby measuring changes in polarization) with voltage-clamp and patch-clamp techniques, *e.g.*, the “cell-attached” mode, the “inside-out” mode, and the “whole cell” mode (*see, e.g.*, Ackerman *et al.*, *New Engl. J. Med.* 336:1575-1595 (1997)). Whole cell currents are conveniently determined using the standard methodology (*see, e.g.*, Hamil *et al.*, *Pflugers. Archiv.* 391:85 (1981). Other known assays include: radiolabeled ion flux assays and fluorescence assays using voltage-sensitive dyes (*see, e.g.*, Vestergaard-Bogind *et al.*, *J. Membrane Biol.* 88:67-75 (1988); Gonzales & Tsien, *Chem. Biol.* 4:269-277 (1997); Daniel *et al.*, *J. Pharmacol. Meth.* 25:185-193 (1991); Holevinsky *et al.*, *J. Membrane Biology* 137:59-70 (1994)). Generally, the compounds to be tested are present in the range from 1 pM to 100 mM.

The effects of the test compounds upon the function of the polypeptides can be measured by examining any of the parameters described above. Any suitable physiological change that affects GPCR activity can be used to assess the influence of a test compound on the polypeptides of this invention. When the functional consequences are determined using intact cells or animals, one can also measure a variety of effects such as transmitter release, hormone release, transcriptional changes to both known and uncharacterized genetic markers (*e.g.*, northern blots), changes in cell metabolism such as cell growth or pH changes, and changes in intracellular second messengers such as Ca²⁺, IP3, cGMP, or cAMP.

Preferred assays for G-protein coupled receptors include cells that are loaded with ion or voltage sensitive dyes to report receptor activity. Assays for determining activity of such receptors can also use known agonists and antagonists for other G-protein coupled receptors as negative or positive controls to assess activity of tested compounds. In assays for identifying modulatory compounds (*e.g.*, agonists, antagonists), changes in the level of ions in the cytoplasm or membrane voltage will be monitored using an ion sensitive or membrane voltage fluorescent indicator, respectively. Among the ion-sensitive indicators and voltage probes that may be employed are those disclosed in the Molecular Probes 1997 Catalog. For G-protein coupled receptors, promiscuous G-proteins such as Gα15 and Gα16 can be used in the assay of choice

(Wilkie *et al.*, *Proc. Nat'l Acad. Sci. USA* 88:10049-10053 (1991)). Such promiscuous G-proteins allow coupling of a wide range of receptors.

Receptor activation typically initiates subsequent intracellular events, *e.g.*, increases in second messengers such as IP₃, which releases intracellular stores of calcium ions. Activation of some G-protein coupled receptors stimulates the formation of inositol triphosphate (IP₃) through phospholipase C-mediated hydrolysis of phosphatidylinositol (Berridge & Irvine, *Nature* 312:315-21 (1984)). IP₃ in turn stimulates the release of intracellular calcium ion stores. Thus, a change in cytoplasmic calcium ion levels, or a change in second messenger levels such as IP₃ can be used to assess G-protein coupled receptor function. Cells expressing such G-protein coupled receptors may exhibit increased cytoplasmic calcium levels as a result of contribution from both intracellular stores and via activation of ion channels, in which case it may be desirable although not necessary to conduct such assays in calcium-free buffer, optionally supplemented with a chelating agent such as EGTA, to distinguish fluorescence response resulting from calcium release from internal stores.

Other assays can involve determining the activity of receptors which, when activated, result in a change in the level of intracellular cyclic nucleotides, *e.g.*, cAMP or cGMP, by activating or inhibiting enzymes such as adenylate cyclase. There are cyclic nucleotide-gated ion channels, *e.g.*, rod photoreceptor cell channels and olfactory neuron channels that are permeable to cations upon activation by binding of cAMP or cGMP (*see, e.g.*, Altenhofen *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* 88:9868-9872 (1991) and Dhallan *et al.*, *Nature* 347:184-187 (1990)). In cases where activation of the receptor results in a decrease in cyclic nucleotide levels, it may be preferable to expose the cells to agents that increase intracellular cyclic nucleotide levels, *e.g.*, forskolin, prior to adding a receptor-activating compound to the cells in the assay. Cells for this type of assay can be made by co-transfection of a host cell with DNA encoding a cyclic nucleotide-gated ion channel, GPCR phosphatase and DNA encoding a receptor (*e.g.*, certain glutamate receptors, muscarinic acetylcholine receptors, dopamine receptors, serotonin receptors, and the like), which, when activated, causes a change in cyclic nucleotide levels in the cytoplasm.

In a preferred embodiment, T2R protein activity is measured by expressing a T2R gene in a heterologous cell with a promiscuous G-protein that links the receptor to a phospholipase C signal transduction pathway (*see* Offermanns & Simon, *J. Biol. Chem.* 270:15175-15180 (1995)). Optionally the cell line is HEK-293 (which does not naturally

express T2R genes) and the promiscuous G-protein is G α 15 (Offermanns & Simon, *supra*). Modulation of taste transduction is assayed by measuring changes in intracellular Ca²⁺ levels, which change in response to modulation of the T2R signal transduction pathway via administration of a molecule that associates with a T2R protein. Changes in Ca²⁺ levels are optionally measured using fluorescent Ca²⁺ indicator dyes and fluorometric imaging.

In one embodiment, the changes in intracellular cAMP or cGMP can be measured using immunoassays. The method described in Offermanns & Simon, *J. Biol. Chem.* 270:15175-15180 (1995) may be used to determine the level of cAMP. Also, the method described in Felley-Bosco *et al.*, *Am. J. Resp. Cell and Mol. Biol.* 11:159-164 (1994) may be used to determine the level of cGMP. Further, an assay kit for measuring cAMP and/or cGMP is described in U.S. Patent 4,115,538, herein incorporated by reference.

In another embodiment, phosphatidyl inositol (PI) hydrolysis can be analyzed according to U.S. Patent 5,436,128, herein incorporated by reference. Briefly, the assay involves labeling of cells with ³H-myoinositol for 48 or more hrs. The labeled cells are treated with a test compound for one hour. The treated cells are lysed and extracted in chloroform-methanol-water after which the inositol phosphates were separated by ion exchange chromatography and quantified by scintillation counting. Fold stimulation is determined by calculating the ratio of cpm in the presence of agonist to cpm in the presence of buffer control. Likewise, fold inhibition is determined by calculating the ratio of cpm in the presence of antagonist to cpm in the presence of buffer control (which may or may not contain an agonist).

In another embodiment, transcription levels can be measured to assess the effects of a test compound on signal transduction. A host cell containing a T2R protein of interest is contacted with a test compound for a sufficient time to effect any interactions, and then the level of gene expression is measured. The amount of time to effect such interactions may be empirically determined, such as by running a time course and measuring the level of transcription as a function of time. The amount of transcription may be measured by using any method known to those of skill in the art to be suitable. For example, mRNA expression of the protein of interest may be detected using northern blots or their polypeptide products may be identified using immunoassays. Alternatively, transcription based assays using reporter gene may be used as described in U.S. Patent

5,436,128, herein incorporated by reference. The reporter genes can be, *e.g.*, chloramphenicol acetyltransferase, luciferase, β -galactosidase and alkaline phosphatase. Furthermore, the protein of interest can be used as an indirect reporter via attachment to a second reporter such as green fluorescent protein (*see, e.g.*, Mistili & Spector, *Nature Biotechnology* 15:961-964 (1997)).

The amount of transcription is then compared to the amount of transcription in either the same cell in the absence of the test compound, or it may be compared with the amount of transcription in a substantially identical cell that lacks the protein of interest. A substantially identical cell may be derived from the same cells from which the recombinant cell was prepared but which had not been modified by introduction of heterologous DNA. Any difference in the amount of transcription indicates that the test compound has in some manner altered the activity of the protein of interest.

B. Modulators

The compounds tested as modulators of a T2R family member can be any small chemical compound, or a biological entity, such as a protein, sugar, nucleic acid or lipid. Alternatively, modulators can be genetically altered versions of a T2R gene. Typically, test compounds will be small chemical molecules and peptides. Essentially any chemical compound can be used as a potential modulator or ligand in the assays of the invention, although most often compounds can be dissolved in aqueous or organic (especially DMSO-based) solutions are used. The assays are designed to screen large chemical libraries by automating the assay steps and providing compounds from any convenient source to assays, which are typically run in parallel (*e.g.*, in microtiter formats on microtiter plates in robotic assays). It will be appreciated that there are many suppliers of chemical compounds, including Sigma (St. Louis, MO), Aldrich (St. Louis, MO), Sigma-Aldrich (St. Louis, MO), Fluka Chemika-Biochemica Analytika (Buchs, Switzerland) and the like.

In one preferred embodiment, high throughput screening methods involve providing a combinatorial chemical or peptide library containing a large number of potential therapeutic compounds (potential modulator or ligand compounds). Such “combinatorial chemical libraries” or “ligand libraries” are then screened in one or more assays, as described herein, to identify those library members (particular chemical species

or subclasses) that display a desired characteristic activity. The compounds thus identified can serve as conventional "lead compounds" or can themselves be used as potential or actual therapeutics.

5 A combinatorial chemical library is a collection of diverse chemical compounds generated by either chemical synthesis or biological synthesis, by combining a number of chemical "building blocks" such as reagents. For example, a linear combinatorial chemical library such as a polypeptide library is formed by combining a set of chemical building blocks (amino acids) in every possible way for a given compound length (i.e., the number of amino acids in a polypeptide compound). Millions of chemical
10 compounds can be synthesized through such combinatorial mixing of chemical building blocks.

Preparation and screening of combinatorial chemical libraries is well known to those of skill in the art. Such combinatorial chemical libraries include, but are not limited to, peptide libraries (*see, e.g.,* U.S. Patent 5,010,175, Furka, *Int. J. Pept. Prot. Res.* 37:487-493 (1991) and Houghton *et al.*, *Nature* 354:84-88 (1991)). Other
15 chemistries for generating chemical diversity libraries can also be used. Such chemistries include, but are not limited to: peptoids (*e.g.,* PCT Publication No. WO 91/19735), encoded peptides (*e.g.,* PCT Publication WO 93/20242), random bio-oligomers (*e.g.,* PCT Publication No. WO 92/00091), benzodiazepines (*e.g.,* U.S. Pat. No. 5,288,514),
20 diversomers such as hydantoins, benzodiazepines and dipeptides (Hobbs *et al.*, *Proc. Nat. Acad. Sci. USA* 90:6909-6913 (1993)), vinylogous polypeptides (Hagihara *et al.*, *J. Amer. Chem. Soc.* 114:6568 (1992)), nonpeptidal peptidomimetics with glucose scaffolding (Hirschmann *et al.*, *J. Amer. Chem. Soc.* 114:9217-9218 (1992)), analogous organic
syntheses of small compound libraries (Chen *et al.*, *J. Amer. Chem. Soc.* 116:2661
25 (1994)), oligocarbamates (Cho *et al.*, *Science* 261:1303 (1993)), and/or peptidyl phosphonates (Campbell *et al.*, *J. Org. Chem.* 59:658 (1994)), nucleic acid libraries (*see* Ausubel, Berger and Sambrook, all *supra*), peptide nucleic acid libraries (*see, e.g.,* U.S. Patent 5,539,083), antibody libraries (*see, e.g.,* Vaughn *et al.*, *Nature Biotechnology*,
14(3):309-314 (1996) and PCT/US96/10287), carbohydrate libraries (*see, e.g.,* Liang *et al.*, *Science*, 274:1520-1522 (1996) and U.S. Patent 5,593,853), small organic molecule
30 libraries (*see, e.g.,* benzodiazepines, Baum C&EN, Jan 18, page 33 (1993); isoprenoids, U.S. Patent 5,569,588; thiazolidinones and metathiazanones, U.S. Patent 5,549,974; pyrrolidines, U.S. Patents 5,525,735 and 5,519,134; morpholino compounds, U.S. Patent 5,506,337; benzodiazepines, 5,288,514, and the like).

Devices for the preparation of combinatorial libraries are commercially available (*see, e.g.*, 357 MPS, 390 MPS, Advanced Chem Tech, Louisville KY, Symphony, Rainin, Woburn, MA, 433A Applied Biosystems, Foster City, CA, 9050 Plus, Millipore, Bedford, MA). In addition, numerous combinatorial libraries are themselves
5 commercially available (*see, e.g.*, ComGenex, Princeton, N.J., Tripos, Inc., St. Louis, MO, 3D Pharmaceuticals, Exton, PA, Martek Biosciences, Columbia, MD, etc.).

C. Solid state and soluble high throughput assays

In one embodiment the invention provide soluble assays using molecules
10 such as a domain such as ligand binding domain, an extracellular domain, a transmembrane domain (*e.g.*, one comprising seven transmembrane regions and cytosolic loops), the transmembrane domain and a cytoplasmic domain, an active site, a subunit association region, *etc.*; a domain that is covalently linked to a heterologous protein to create a chimeric molecule; a T2R protein; or a cell or tissue expressing a T2R protein,
15 either naturally occurring or recombinant. In another embodiment, the invention provides solid phase based *in vitro* assays in a high throughput format, where the domain, chimeric molecule, T2R protein, or cell or tissue expressing the T2R is attached to a solid phase substrate.

In the high throughput assays of the invention, it is possible to screen up to
20 several thousand different modulators or ligands in a single day. In particular, each well of a microtiter plate can be used to run a separate assay against a selected potential modulator, or, if concentration or incubation time effects are to be observed, every 5-10 wells can test a single modulator. Thus, a single standard microtiter plate can assay about 100 (*e.g.*, 96) modulators. If 1536 well plates are used, then a single plate can easily
25 assay from about 100- about 1500 different compounds. It is possible to assay several different plates per day; assay screens for up to about 6,000-20,000 different compounds is possible using the integrated systems of the invention. More recently, microfluidic approaches to reagent manipulation have been developed.

The molecule of interest can be bound to the solid state component,
30 directly or indirectly, via covalent or non covalent linkage, *e.g.*, via a tag. The tag can be any of a variety of components. In general, a molecule which binds the tag (a tag binder) is fixed to a solid support, and the tagged molecule of interest (*e.g.*, the taste transduction molecule of interest) is attached to the solid support by interaction of the tag and the tag binder.

A number of tags and tag binders can be used, based upon known molecular interactions well described in the literature. For example, where a tag has a natural binder, for example, biotin, protein A, or protein G, it can be used in conjunction with appropriate tag binders (avidin, streptavidin, neutravidin, the Fc region of an immunoglobulin, *etc.*) Antibodies to molecules with natural binders such as biotin are also widely available and appropriate tag binders; *see*, SIGMA Immunochemicals 1998 catalogue SIGMA, St. Louis MO).

Similarly, any haptenic or antigenic compound can be used in combination with an appropriate antibody to form a tag/tag binder pair. Thousands of specific antibodies are commercially available and many additional antibodies are described in the literature. For example, in one common configuration, the tag is a first antibody and the tag binder is a second antibody which recognizes the first antibody. In addition to antibody-antigen interactions, receptor-ligand interactions are also appropriate as tag and tag-binder pairs. For example, agonists and antagonists of cell membrane receptors (e.g., cell receptor-ligand interactions such as transferrin, c-kit, viral receptor ligands, cytokine receptors, chemokine receptors, interleukin receptors, immunoglobulin receptors and antibodies, the cadherein family, the integrin family, the selectin family, and the like; *see*, e.g., Pigott & Power, *The Adhesion Molecule Facts Book I* (1993). Similarly, toxins and venoms, viral epitopes, hormones (e.g., opiates, steroids, *etc.*), intracellular receptors (e.g., which mediate the effects of various small ligands, including steroids, thyroid hormone, retinoids and vitamin D; peptides), drugs, lectins, sugars, nucleic acids (both linear and cyclic polymer configurations), oligosaccharides, proteins, phospholipids and antibodies can all interact with various cell receptors.

Synthetic polymers, such as polyurethanes, polyesters, polycarbonates, polyureas, polyamides, polyethyleneimines, polyarylene sulfides, polysiloxanes, polyimides, and polyacetates can also form an appropriate tag or tag binder. Many other tag/tag binder pairs are also useful in assay systems described herein, as would be apparent to one of skill upon review of this disclosure.

Common linkers such as peptides, polyethers, and the like can also serve as tags, and include polypeptide sequences, such as poly gly sequences of between about 5 and 200 amino acids. Such flexible linkers are known to persons of skill in the art. For example, poly(ethylene glycol) linkers are available from Shearwater Polymers, Inc. Huntsville, Alabama. These linkers optionally have amide linkages, sulfhydryl linkages, or heterofunctional linkages.

Tag binders are fixed to solid substrates using any of a variety of methods currently available. Solid substrates are commonly derivatized or functionalized by exposing all or a portion of the substrate to a chemical reagent which fixes a chemical group to the surface which is reactive with a portion of the tag binder. For example, groups which are suitable for attachment to a longer chain portion would include amines, hydroxyl, thiol, and carboxyl groups. Aminoalkylsilanes and hydroxyalkylsilanes can be used to functionalize a variety of surfaces, such as glass surfaces. The construction of such solid phase biopolymer arrays is well described in the literature. See, e.g., Merrifield, *J. Am. Chem. Soc.* 85:2149-2154 (1963) (describing solid phase synthesis of, e.g., peptides); Geysen *et al.*, *J. Immun. Meth.* 102:259-274 (1987) (describing synthesis of solid phase components on pins); Frank & Doring, *Tetrahedron* 44:6031-6040 (1988) (describing synthesis of various peptide sequences on cellulose disks); Fodor *et al.*, *Science*, 251:767-777 (1991); Sheldon *et al.*, *Clinical Chemistry* 39(4):718-719 (1993); and Kozal *et al.*, *Nature Medicine* 2(7):753-759 (1996) (all describing arrays of biopolymers fixed to solid substrates). Non-chemical approaches for fixing tag binders to substrates include other common methods, such as heat, cross-linking by UV radiation, and the like.

D. Computer-based assays

Yet another assay for compounds that modulate T2R protein activity involves computer assisted drug design, in which a computer system is used to generate a three-dimensional structure of a T2R protein based on the structural information encoded by its amino acid sequence. The input amino acid sequence interacts directly and actively with a preestablished algorithm in a computer program to yield secondary, tertiary, and quaternary structural models of the protein. The models of the protein structure are then examined to identify regions of the structure that have the ability to bind, e.g., ligands. These regions are then used to identify ligands that bind to the protein.

The three-dimensional structural model of the protein is generated by entering protein amino acid sequences of at least 10 amino acid residues or corresponding nucleic acid sequences encoding a T2R polypeptide into the computer system. The nucleotide sequence encoding the polypeptide, or the amino acid sequence thereof, can be any of SEQ ID NO:1-165, and conservatively modified versions thereof. The amino acid sequence represents the primary sequence or subsequence of the protein, which encodes the structural information of the protein. At least 10 residues of the amino acid sequence

(or a nucleotide sequence encoding 10 amino acids) are entered into the computer system from computer keyboards, computer readable substrates that include, but are not limited to, electronic storage media (*e.g.*, magnetic diskettes, tapes, cartridges, and chips), optical media (*e.g.*, CD ROM), information distributed by internet sites, and by RAM. The
5 three-dimensional structural model of the protein is then generated by the interaction of the amino acid sequence and the computer system, using software known to those of skill in the art.

The amino acid sequence represents a primary structure that encodes the information necessary to form the secondary, tertiary and quaternary structure of the
10 protein of interest. The software looks at certain parameters encoded by the primary sequence to generate the structural model. These parameters are referred to as “energy terms,” and primarily include electrostatic potentials, hydrophobic potentials, solvent accessible surfaces, and hydrogen bonding. Secondary energy terms include van der Waals potentials. Biological molecules form the structures that minimize the energy
15 terms in a cumulative fashion. The computer program is therefore using these terms encoded by the primary structure or amino acid sequence to create the secondary structural model.

The tertiary structure of the protein encoded by the secondary structure is then formed on the basis of the energy terms of the secondary structure. The user at this
20 point can enter additional variables such as whether the protein is membrane bound or soluble, its location in the body, and its cellular location, *e.g.*, cytoplasmic, surface, or nuclear. These variables along with the energy terms of the secondary structure are used to form the model of the tertiary structure. In modeling the tertiary structure, the computer program matches hydrophobic faces of secondary structure with like, and
25 hydrophilic faces of secondary structure with like.

Once the structure has been generated, potential ligand binding regions are identified by the computer system. Three-dimensional structures for potential ligands are generated by entering amino acid or nucleotide sequences or chemical formulas of compounds, as described above. The three-dimensional structure of the potential ligand
30 is then compared to that of the T2R protein to identify ligands that bind to the protein. Binding affinity between the protein and ligands is determined using energy terms to determine which ligands have an enhanced probability of binding to the protein.

Computer systems are also used to screen for mutations, polymorphic variants, alleles and interspecies homologs of T2R genes. Such mutations can be

associated with disease states or genetic traits. As described above, GeneChip™ and related technology can also be used to screen for mutations, polymorphic variants, alleles and interspecies homologs. Once the variants are identified, diagnostic assays can be used to identify patients having such mutated genes. Identification of the mutated T2R genes involves receiving input of a first nucleic acid or amino acid sequence of a T2R gene, *e.g.*, any of SEQ ID NO:1-165, or conservatively modified versions thereof. The sequence is entered into the computer system as described above. The first nucleic acid or amino acid sequence is then compared to a second nucleic acid or amino acid sequence that has substantial identity to the first sequence. The second sequence is entered into the computer system in the manner described above. Once the first and second sequences are compared, nucleotide or amino acid differences between the sequences are identified. Such sequences can represent allelic differences in various T2R genes, and mutations associated with disease states and genetic traits.

IX. Administration and pharmaceutical compositions

Taste modulators can be administered directly to the mammalian subject for modulation of taste, *e.g.*, modulation of bitter taste, *in vivo*. Administration is by any of the routes normally used for introducing a modulator compound into ultimate contact with the tissue to be treated, optionally the tongue or mouth. The taste modulators are administered in any suitable manner, optionally with pharmaceutically acceptable carriers. Suitable methods of administering such modulators are available and well known to those of skill in the art, and, although more than one route can be used to administer a particular composition, a particular route can often provide a more immediate and more effective reaction than another route.

Pharmaceutically acceptable carriers are determined in part by the particular composition being administered, as well as by the particular method used to administer the composition. Accordingly, there is a wide variety of suitable formulations of pharmaceutical compositions of the present invention (*see, e.g., Remington's Pharmaceutical Sciences*, 17th ed. 1985)).

The taste modulators, alone or in combination with other suitable components, can be made into aerosol formulations (*i.e.*, they can be "nebulized") to be administered via inhalation. Aerosol formulations can be placed into pressurized acceptable propellants, such as dichlorodifluoromethane, propane, nitrogen, and the like.

Formulations suitable for administration include aqueous and non-aqueous solutions, isotonic sterile solutions, which can contain antioxidants, buffers, bacteriostats, and solutes that render the formulation isotonic, and aqueous and non-aqueous sterile suspensions that can include suspending agents, solubilizers, thickening agents, stabilizers, and preservatives. In the practice of this invention, compositions can be administered, for example, by orally, topically, intravenously, intraperitoneally, intravesically or intrathecally. Optionally, the compositions are administered orally or nasally. The formulations of compounds can be presented in unit-dose or multi-dose sealed containers, such as ampules and vials. Solutions and suspensions can be prepared from sterile powders, granules, and tablets of the kind previously described. The modulators can also be administered as part a of prepared food or drug.

The dose administered to a patient, in the context of the present invention should be sufficient to effect a beneficial response in the subject over time. The dose will be determined by the efficacy of the particular taste modulators employed and the condition of the subject, as well as the body weight or surface area of the area to be treated. The size of the dose also will be determined by the existence, nature, and extent of any adverse side-effects that accompany the administration of a particular compound or vector in a particular subject.

In determining the effective amount of the modulator to be administered in a physician may evaluate circulating plasma levels of the modulator, modulator toxicities,, and the production of anti-modulator antibodies. In general, the dose equivalent of a modulator is from about 1 ng/kg to 10 mg/kg for a typical subject.

For administration, taste modulators of the present invention can be administered at a rate determined by the LD-50 of the modulator, and the side-effects of the inhibitor at various concentrations, as applied to the mass and overall health of the subject. Administration can be accomplished via single or divided doses.

VIII. Kits

T2R genes and their homologs are useful tools for identifying taste receptor cells, for forensics and paternity determinations, and for examining taste transduction. T2R family member-specific reagents that specifically hybridize to T2R nucleic acids, such as T2R probes and primers, and T2R specific reagents that specifically bind to a T2R protein, *e.g.*, T2R antibodies are used to examine taste cell expression and taste transduction regulation.

Nucleic acid assays for the presence of DNA and RNA for a T2R family member in a sample include numerous techniques are known to those skilled in the art, such as Southern analysis, northern analysis, dot blots, RNase protection, S1 analysis, amplification techniques such as PCR and LCR, and *in situ* hybridization. In *in situ* hybridization, for example, the target nucleic acid is liberated from its cellular surroundings in such as to be available for hybridization within the cell while preserving the cellular morphology for subsequent interpretation and analysis. The following articles provide an overview of the art of *in situ* hybridization: Singer *et al.*, *Biotechniques* 4:230-250 (1986); Haase *et al.*, *Methods in Virology*, vol. VII, pp. 189-226 (1984); and *Nucleic Acid Hybridization: A Practical Approach* (Hames *et al.*, eds. 1987). In addition, a T2R protein can be detected with the various immunoassay techniques described above. The test sample is typically compared to both a positive control (*e.g.*, a sample expressing a recombinant T2R protein) and a negative control.

The present invention also provides for kits for screening for modulators of T2R family members. Such kits can be prepared from readily available materials and reagents. For example, such kits can comprise any one or more of the following materials: T2R nucleic acids or proteins, reaction tubes, and instructions for testing T2R activity. Optionally, the kit contains a biologically active T2R receptor. A wide variety of kits and components can be prepared according to the present invention, depending upon the intended user of the kit and the particular needs of the user.

EXAMPLES

The following examples are provided by way of illustration only and not by way of limitation. Those of skill in the art will readily recognize a variety of noncritical parameters that could be changed or modified to yield essentially similar results.

Example I--Identification of the T2R gene family

Recent genetic linkage studies in humans identified a locus at 5p15 that is associated with the ability to respond to the bitter substance 6-n-propyl-2-thiouracil (PROP; Reed *et al.*, *Am. J. Hum. Genet.* 64:1478-1480 (1999)). To determine whether differences in PROP sensitivity reflected functional differences in a bitter taste receptor, DNA sequence databases were searched for genes encoding candidate transmembrane proteins at this location. Analysis of open reading frames in 450 kb of DNA spanning six

sequenced human genomic BAC clones(see, e.g., accession number AC003015) from this interval identified a novel GPCR (T2R1) at 5p15.2. T2R1 has seven putative transmembrane segments as well as several conserved residues often present in GPCRs (Probst *et al.*, *DNA Cell. Biol.* 11:1-20 (1992)).

5 Computer searches using T2R1, and reiterated with T2R1-related sequences, revealed 19 additional human receptors (12 full-length and 7 pseudogenes). Full-length hT2Rs were isolated by PCR amplification of genomic DNA. Full-length hT2Rs were used to probe a rat circumvallate cDNA library (Hoon *et al.*, *Cell*, 96:541-551 (1999)) and mouse BAC filter arrays (Genome Systems) at low stringency (50-55 °C
10 wash in 1 X SSC). Southern hybridization experiments were used to identify a non-redundant set of positive BACs and to order overlapping BACs.

 These new receptors, referred to as T2Rs (also known as "SF"), define a novel family of GPCRs that are distantly related to V1R vomeronasal receptors and opsins. In contrast to T1Rs, which belong to the superfamily of GPCRs characterized by
15 a large N-terminal domain (Hoon *et al.*, *Cell*, 96:541-551 (1999)), the T2Rs have only a short extracellular N-terminus. Individual members of the T2R-family exhibit 30-70% amino acid identity, and most share highly conserved sequence motifs in the first three and last transmembrane segments, and also in the second cytoplasmic loop. The most divergent regions between T2Rs are the extracellular segments, extending partway into
20 the transmembrane helices. Presumably, the high degree of variability between T2Rs reflects the need to recognize many structurally diverse ligands. Like many other GPCR genes, T2Rs do not contain introns that interrupt coding regions.

Example II--Organization of human T2R genes.

25 The identified human T2R genes are localized on three chromosomes, and are often organized as head-to-tail arrays. For example, four receptor genes are clustered within a single PAC clone from 7q31 and nine in a BAC clone from 12p13. There may be more human T2Rs in these arrays, as several additional human T2Rs were found within partially sequenced BAC clones that overlap the 9 gene T2R cluster. Within a
30 given array, the similarity of receptors is highly variable, including both relatively related (e.g. hT2R13, hT2R14 and hT2R15), and highly divergent receptors (e.g. hT2R3 and hT2R4). This type of organization is mirrored in the mouse (see below), and resembles the genomic organization that has been observed for olfactory receptor genes in humans, mice, flies and worms (Rouquier *et al.*, *Nat. Genet.* 18:243-250 (1998)); Sullivan *et al.*,

PNAS 93:884-888 (1996)); Clyne *et al.*, *Neuron* 22:327-388 (1999)); Vosshall *et al.*, *Cell* 96:725-736 (1999)); Troemel *et al.*, *Cell* 83:207-218 (1995)).

To obtain estimates of the size of this gene family, various genomic resources were examined. Analysis of the Genome Sequence Survey database (gss) yielded 12 partial T2R sequences. Because this database represents an essentially random sampling of ~14% of the human genome, this number suggests that there may be ~90 T2R genes in the human genome. Similar searches of the finished (nr) and unfinished high-throughput human genomic sequence databases (htgs) produced 36 full-length and 15 partial T2R sequences. These databases contain ~50% of the genome sequence, also pointing to ~100 T2R genes in the genome. Recognizing that this analysis may be inaccurate due to the quality of the available databases, and the clustered, non-random distribution of T2Rs in the human genome, it is estimated that the T2R family consists of between 80 to 120 members. However, more than 1/3 of the full-length human T2Rs are pseudogenes; thus, the final number of functional human receptors may be significantly smaller (*i.e.*, 40-80). This is similar to what has been observed for human olfactory receptors, where many of the genes appear to be pseudogenes (Rouquier *et al.*, *Nat. Genet.* 18:243-250 (1998)).

Example III--T2R genes are linked to loci involved in bitter taste

The genetics of sweet and bitter tasting has been extensively studied in mice, where a number of loci influencing responses to sweet and bitter tastants have been mapped by behavioral taste-choice assays (Warren and Lewis, *Nature* 227:77-78 (1970)); Fuller, *J. Hered.* 65:33-66 (1974)). The distal end of mouse chromosome 6 contains a cluster of bitter genes that includes *Soa* (for sucrose octaacetate; Capeless *et al.*, *Behav. Genet.* 22:655-663 (1992)), *Rua* (raffinose undecaacetate; Lush, *Genet. Res.* 47:117-123 (1986)), *Cyx* (cycloheximide; Lush and Holland, *Genet. Res.* 52:207-212 (1988)) and *Qui* (quinine; Lush, *Genet. Res.* 44:151-160 (1984)). Recombination studies indicated that these four loci are closely linked to each other, and to *Prp* (salivary proline rich protein; Azen *et al.*, *Trends Genet.* 2:199-200 (1986)). The human 9 gene T2R cluster contains three interspersed *PRP* genes, and maps to an interval that is homologous with the mouse chromosome 6 bitter cluster.

To define the relationship between the mouse chromosome 6 bitter cluster and T2Rs, a large number of mouse T2R genes were isolated and their genomic organization and physical and genetic map locations were determined. By screening

mouse genomic libraries with human T2Rs, 61 BAC-clones containing 28 mouse T2Rs were isolated. The mouse and human receptors display significant amino acid sequence divergence, but share the sequence motifs common to members of this novel family of receptors. Mouse T2Rs were mapped using a mouse/hamster radiation hybrid panel (Research Genetics), and by examining the strain distribution pattern of single nucleotide polymorphisms in a panel of C57BL/6J x DBA/2J recombinant inbred lines (Jackson Laboratory). These studies showed that the mouse genes are clustered at only a few genomic locations. Each genomic interval containing mouse T2Rs is homologous to one containing its closest human counterpart: mT2R8 and hT2R4, mT2R18 and hT2R16, and mT2R19 and hT2R1. Of these 3 sets of potentially orthologous pairs of human/mouse receptors, both the human T2R1 and T2R16 genes map to locations implicated in human bitter perception (Conneally *et al.*, *Hum. Hered.* 26:267-271 (1976); Reed *et al.*, *Am. J. Hum. Genet.* 64:1478-1480 (1999)). The remaining 25 mT2Rs all map to the distal end of chromosome 6, and are represented by 3 BAC contigs spanning at least 400 kb.

Since *Prp* and the bitter-cluster also map to the distal end of mouse chromosome 6, it was determined whether they *localize* within this array of T2Rs. Analysis of a DBA/2 x C57BL/6 recombinant inbred panel revealed that receptors within all 3 BAC-contigs co-segregate with *Prp* and the bitter cluster. Further, the mouse *Prp* gene was isolated (accession number M23236, containing *D6Mit13*) and shown that it lies within the large chromosome 6 T2R cluster. These results demonstrate that T2Rs are intimately linked to loci implicated in bitter perception.

Example IV--T2Rs are expressed in taste receptor cells

The lingual epithelium contains taste buds in three types of papillae: circumvallate papillae at the very back of the tongue, foliate papillae at the posterior lateral edge of the tongue, and fungiform papillae *dispersed* throughout the front half of the tongue surface. Other parts of the oral cavity also have taste buds; these are particularly prominent in the palate epithelium in an area known as the geschmackstreifen and in the epiglottis. To examine the patterns of expression of T2Rs, *in situ* hybridizations were performed using sections of various taste papillae. To ensure that the probes used were expressed in taste tissue, a rat circumvallate cDNA library was screened, leading to the isolation of 14 rat T2Rs cDNAs, each of which is an ortholog of a mouse genomic clone.

To carry out the *in situ* hybridization, tissue was obtained from adult rats and mice. No sex-specific differences of expression patterns were observed, therefore male and female animals were used interchangeably. Fresh frozen sections (16 μ m) were attached to silanized slides and prepared for *in situ* hybridization as described previously (Hoon *et al.*, *Cell*, 96:541-551 (1999)). All *in situ* hybridizations were carried out at high stringency (hybridization, 5 X SSC, 50% formamide, 65-72°C; washing, 0.2 X SSC, 72°C). Signals were developed using alkaline-phosphatase conjugated antibodies to digoxigenin and standard chromogenic substrates (Boehringer Mannheim). Where possible, probes contained extensive 3'-non translated sequence to minimize potential cross-hybridization between T2Rs, which was not observed at the stringency used for *in situ* hybridization.

These experiments demonstrated that T2Rs are selectively expressed in subsets of taste receptor cells of the tongue and palate epithelium. Each receptor hybridizes to an average of 2 cells per taste bud per section. Since the sections used in these experiments contain 1/5-1/3 the depth of a taste bud, this reflects a total of 6-10 positive cells/taste bud/probe (or about 15% of the cells in a taste bud). Examination of serial sections demonstrated that all of the taste buds of the circumvallate papilla contain cells that are positive for each of these probes. Thus far, comparable results have been observed with 11 rat T2Rs, and in mouse sections hybridized with 17 different mT2R probes.

Similar studies in foliate, geschmackstreifen and epiglottis taste buds demonstrated that each receptor probe also labels approximately 15% of the cells in every taste bud. In contrast, T2Rs are rarely expressed in fungiform papillae. Examination of hundreds of fungiform taste buds using 11 different T2R probes demonstrated that less than 10% of all fungiform papillae contain T2R-expressing cells. Interestingly, the few fungiform taste buds that do express T2Rs regularly contain multiple positive cells. In fact, the number of positive cells in these papillae is not significantly different from that seen in taste buds from other regions of the oral cavity. Furthermore, fungiform papillae that contain T2R-expressing cells generally appear clustered. This unexpected finding may provide an important clue about the logic of taste coding. It is known that single fibers of the chorda tympani nerve innervate multiple cells in a fungiform taste bud, and that the same fiber often projects to neighboring papillae (Miller, *J. Comp. Neurol.* 158:155-166 (1974)). Perhaps the non-random distribution of T2R-positive taste receptor

cells and taste buds in fungiform papillae reflect a map of connectivity between similar cells.

Northern analysis and *in situ* hybridization demonstrated that T2Rs are not widely expressed outside taste tissue.

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Example V--Individual receptor cells express multiple T2R receptors

The above-described results demonstrated that any given T2R is expressed in ~15% of the cells of circumvallate, foliate and palate taste buds. Given that there are over 30 T2Rs in the rodent genome, a taste cell must express more than one receptor. To determine how many receptors are expressed in any cell, and what fraction of taste receptor cells express T2Rs, the number of circumvallate cells labeled with various mixes of 2, 5 or 10 receptors was compared with those labeled with the corresponding individual probes. By counting positive cells in multiple serial sections, it was determined that the number of taste cells labeled with the mixed probes (~20%) was only slightly larger than that labeled by any individual receptor (~15%). Not surprisingly, the signal intensity was significantly enhanced in the mixed probe hybridizations. Similar results were observed in taste buds from other regions of the oral cavity including the fungiform papillae. To directly demonstrate co-expression, double labeling experiments were carried out using a collection of differentially labeled cRNA probes. For double-label fluorescent detection, probes were labeled either with fluorescein or with digoxigenin. An alkaline-phosphatase conjugated anti-fluorescein antibody (Amersham) and a horseradish-peroxidase conjugated anti-digoxigenin antibody were used in combination with fast-red and tyramide fluorogenic substrates (Boehringer Mannheim and New England Nuclear). In these experiments, the majority of cells were found to express multiple receptors.

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Example VI--T2R genes are selectively expressed in gustducin-expressing cells

Previous results had shown that T1Rs are expressed in ~30% of taste receptor cells. *In situ* hybridizations with differentially labeled T1R and T2R probes showed that there is no overlap in the expression of these two classes of receptors. Gustducin is also expressed in a large subset of taste receptor cells, but for the most part is not co-expressed with T1Rs (Hoon *et al.*, *Cell*, 96:541-551 (1999)). To determine if T2Rs are expressed in gustducin cells, *in situ* hybridizations were performed using differentially labeled T2Rs and gustducin riboprobes. These experiments demonstrated

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that T2Rs are exclusively expressed in gustducin-positive cells of the tongue and palate taste buds.

Approximately 1/3 of the gustducin cells in the circumvallate, foliate and palate taste buds did not label with a mix of 10 T2R probes, suggesting that not all gustducin-expressing cells express T2Rs. These cells may express other, perhaps more distantly related receptors, or could be at a different developmental stage. In fungiform taste buds the situation is quite different. Since only 10% of fungiform taste buds contain T2R positive cells, the great majority of gustducin-positive cells in the front of the tongue do not appear to co-express members of the T2R family of receptors. Therefore, there is likely to be an additional set of receptors expressed in the gustducin-positive cells of fungiform papillae.

Example VII--Functional expression of T2Rs

T2Rs were expressed in conjunction with G α 15, a G-protein α -subunit that has been shown to couple a wide range of receptors to phospholipase C β (Offermanns and Simon, *J Biol Chem*, 270:15175-80 (1995); Krautwurst *et al.*, *Cell* 95:917-926 (1998)). In this system, receptor activation leads to increases in intracellular calcium [Ca²⁺]_i, which can be monitored at the single cell level using the FURA-2 calcium-indicator dye (Tsien *et al.*, *Cell Calcium* 6:145-157 (1985)). To test and optimize G α 15 coupling, two different GPCRs, a G α i-coupled μ -opioid receptor (Reisine, *Neuropharm.* 34:463-472 (1995)) and a G α q-coupled mGluR1 receptor (Masu *et al.*, *Nature* 349:760-765 (1991)), were used. Transfection of these receptors into HEK-293 cell produced robust, agonist-selective, and G α 15-dependent Ca²⁺ responses (Figure 1).

A number of studies have shown that many GPCRs, in particular sensory receptors, require specific "chaperones" for maturation and targeting through the secretory pathway (Baker *et al.*, *Embo J* 13:4886-4895 (1994); Dwyer *et al.*, *Cell* 93:455-466 (1998)). Recently, Krautwurst *et al.* (*Cell* 95:917-926 (1998)) generated chimeric receptors consisting of the first 20 amino acids of rhodopsin and various rodent olfactory receptors. These were targeted to the plasma membrane and functioned as odorant receptors in HEK-293 cells. To determine whether rhodopsin sequences can also help target T2Rs to the plasma membrane, rhodopsin-T2R chimeras (rho-T2Rs) were constructed. Expression of these fusion proteins demonstrated that the first 39 amino

acids of bovine rhodopsin are very effective in targeting T2Rs to the plasma membrane of HEK-293 cells (Figure 2). Similar results were obtained with 11 human and 16 rodent T2Rs (see below). To further enhance the level of T2R expression, rho-T2Rs were placed under the control of a strong EF-1 α promoter, and introduced as episomal plasmids into modified HEK-293 cells expressing G α 15 (pEAKrapid cells).

A bridge overlap PCR extension technique was used to generate rho-T2R chimeras, which contain the first 39 amino acids of bovine rhodopsin in frame with human and rodent T2R coding sequences (Mehta and Singh, *Biotechniques* 26:1082-1086 (1999). All receptors were cloned into a pEAK10 mammalian expression vector (Edge Biosystems, MD). Modified HEK-293 cells (PEAK^{rapid} cells; Edge BioSystems, MD) were grown and maintained at 37 °C in UltraCulture medium (Bio Whittaker) supplemented with 5% fetal bovine serum, 100 μ g/ml Gentamycin sulphate (Fisher), 1 μ g/ml Amphotericin B and 2 mM GlutaMax I (Lifetechnologies). For transfection, cells were seeded onto matrigel coated 24-well culture plates or 35 mm recording chambers. After 24 h at 37 °C, cells were washed in OptiMEM medium (Lifetechnologies) and transfected using LipofectAMINE reagent (Lifetechnologies). Transfection efficiencies were estimated by co-transfection of a GFP reporter plasmid, and were typically >70%. Immunofluorescence staining, and activity assays were performed 36-48 h after transfection.

For immunostaining, transfected cells were grown on coated glass coverslips, fixed for 20 min in ice-cold 2% paraformaldehyde, blocked with 1% BSA, and incubated for 4-6 h at 4 °C in blocking buffer containing a 1:1000 dilution of anti-rhodopsin mAb B6-30 (Hargrave, *et al. Exp Eye Res* 42:363-373 (1986)). Chimeric receptor expression was visualized using FITC-coupled donkey anti-mouse secondary antibodies (Jackson Immunochemical).

Two parallel strategies were employed to identify ligands for T2Rs. In one, a random set of human, rat and mouse T2R receptors were selected and individually tested against a collection of 55 bitter and sweet tastants, including (shown with maximum concentrations tested): 5 mM aristolochic acid, 5 mM atropine, 5 mM brucine, 5 mM caffeic acid, 10 mM caffeine, 1 mM chloroquine, 5 mM cycloheximide, 10 mM denatonium benzoate, 5 mM (-) epicatechin, 10 mM L-leucine, 10 mM L-lysine, 10 mM MgCl₂, 5 mM naringin, 10 mM nicotine, 2.5 mM papavarine hydrochloride, 3 mM phenyl thiocarbamide, 10 mM 6-n-propyl thiouracil, 1 mM quinacrine, 1 mM quinine

hydrochloride, 800 μ M raffinose undecaacetate, 3 mM salicin, 5 mM sparteine, 5 mM strychnine nitrate, 3 mM sucrose octaacetate, 2 mM tetraethyl ammonium chloride, 10 mM L-tyrosine, 5 mM yohimbine, 10 mM each of L-glycine, L-alanine, D-tryptophan, L-phenylalanine, L-arginine, sodium saccharin, aspartame, sodium cyclamate, acesulfame K, 150 mM each of sucrose, lactose, maltose, D-glucose, D-fructose, D-galactose, D-sorbitol, 0.1% monellin, 0.1% thaumatin. Additional sweet tastants were 150 μ M alitame, 1.8 mM dulcin, 800 μ M stevioside, 1.9 mM cyanosusan, 600 μ M neohesperidin dihydrochalcone, 10 mM xylitol, 9.7 mM H-Asp-D-Ala-OTMCP, 70 μ M N-Dmb-L-Asp-L-Phe-Ome, and 12 μ M N-Dmb-L-Asp-D-Val(S)- α methylbenzylamide. In these assays, functional coupling was assessed based on four criteria: tastant selectivity, temporal specificity, and receptor- and G protein-dependence. The second strategy relied upon data on the genetics of bitter perception in mice to link candidate receptors with specific tastants.

Nearly 30 years ago, it was first reported that various inbred strains of mice differ in their sensitivity to the bitter compound sucrose-octaacetate (Warren and Lewis, *Nature* 227:77-78 (1970)). Subsequently, a number of studies demonstrated that this strain difference was due to allelic variation at a single genetic locus (Soa) (Whitney and Harder, *Behav Genet* 16:559-574 (1986); Capeless *et al.*, *Behav Genet* 22:655-663 (1992)). These findings were extended to additional loci influencing sensitivity to various bitter tastants, including raffinose undecaacetate (Rua), cycloheximide (Cyx), copper glycinate (Glb), and quinine (Qui) (Lush, *Genet. Res.* 44:151-160 (1984); Lush, *Genet. Res.* 47:117-123 (1986), Lush and Holland, (1988)). Genetic mapping experiments showed that the Soa, Rua, Cyx, Qui and Glb loci are clustered at the distal end of chromosome 6 (Lush and Holland, *Genet. Res.* 52:207-212 (1988); Capeless *et al.*, *Behav Genet* 22:655-663 (1992)). In view of the above-described localization of various T2R genes to bitter-associated loci in mice, T2R receptors from this array were constructed as corresponding rho-mT2R chimeras and individually transfected into HEK-293 cells expressing the promiscuous G α 15 protein. After loading the cells with FURA-2, responses to sucrose octaacetate, raffinose undecaacetate, copper glycinate, quinine, and cycloheximide were assayed.

Transfected cells were washed once in Hank's balanced salt solution with 1 mM sodium pyruvate and 10 mM HEPES, pH 7.4 (assay buffer), and loaded with 2 μ M FURA-2 AM (Molecular Probes) for 1 h at room temperature. The loading solution was

removed and cells were incubated in 200 μ l of assay buffer for 1 h to allow the cleavage of the AM ester. For most experiments, 24-well tissue culture plates containing cells expressing a single rho-T2R were stimulated with 200 μ l of a 2x tastant solution (see next section). $[Ca^{2+}]_i$ changes were monitored using a Nikon Diaphot 200 microscope
 5 equipped with a 10x/0.5 fluor objective with the TILL imaging system (T.I.L.L Photonics GmbH). Acquisition and analysis of the fluorescence images used TILL-Vision software. Generally, $[Ca^{2+}]_i$ was measured for 80 - 120 s by sequentially illuminating cells for 200ms at 340nm and 380nm and monitoring the fluorescence emission at 510nm using a cooled CCD camera. The F_{340}/F_{380} ratio was analyzed to measure $[Ca^{2+}]_i$.

10 Kinetics of activation and deactivation were measured using a bath perfusion system. Cells were seeded onto a 150 μ l microperfusion chamber, and test solutions were pressure-ejected with a picospritzer apparatus (General Valve, Inc.). Flow-rate was adjusted to ensure complete exchange of the bath solution within 4-5 s. In the case of mT2R5, the entire camera field was measured since >70% of the cells
 15 responded to cycloheximide. For mT2R8 and hT2R4, 100 areas of interest in each were averaged for each experiment.

Cells expressing mT2R5 specifically responded to cycloheximide (Figure 3). The response occurred in nearly all transfected cells and was receptor- and $G\alpha_{15}$ -dependent because cells lacking either of these components did not trigger $[Ca^{2+}]_i$
 20 changes, even at 5000-fold higher cycloheximide concentration. As expected for this coupling system, the tastant-induced increase in $[Ca^{2+}]_i$ was due to release from internal stores, since analogous results were obtained in nominally zero $[Ca^{2+}]_{out}$. The activation of mT2R5 by cycloheximide is very selective, as this receptor did not respond to any other tastants, even at concentrations that far exceeded their biologically relevant range of
 25 action (Saroli, *Naturwissenschaften* 71:428-9 (1984); Glendinning, *Behav Neurosci* 113:840-854 (1994))(Figure 4a,b). While cycloheximide is only moderately bitter to humans, it is strongly aversive to rodents with a sensitivity threshold of ~ 0.25 μ M (Kusano *et al.*, *Appl. Exptl. Zool.* 6:40-50 (1971); Lush and Holland, *Genet. Res.* 52:207-212 (1988)). In the cell-based assay described herein, the concentration of cycloheximide
 30 required to induce half-maximal response of mT2R5 was 0.5 μ M, and the threshold was ~ 0.2 μ M (Figure 4c,d). Notably, this dose-response closely matches the sensitivity range of cycloheximide tasting in mice.

To examine the kinetics of the cycloheximide response, rho-mT2R5 transfected cells were placed on a microperfusion chamber and superfused with test solutions under various conditions. The cells showed robust transient responses to micromolar concentrations of cycloheximide that closely follow application of the stimulus (latency <1 s). As expected, when the tastant was removed, [Ca²⁺]_i returned to baseline. A prolonged exposure to cycloheximide (>10 s) resulted in adaptation: a fast increase of [Ca²⁺]_i followed by a gradual, but incomplete decline to the resting level (Figure 4a). Similarly, successive applications of cycloheximide led to significantly reduced responses, indicative of desensitization (Lefkowitz *et al.*, *Cold Spring Harb Symp Quant Biol* 57:127-133 (1992)). This is likely to occur at the level of the receptor, since responses of a control, co-transfected mGluR1 were not altered during the period of cycloheximide desensitization.

To determine whether other T2Rs are also activated by bitter compounds, 11 rhodopsin-tagged human T2R receptors were assayed by individually transfecting them into HEK-293 cells expressing Gα15. Each transfected line was tested against a battery of bitter and sweet tastants, including amino acids, peptides, and other natural and synthetic compounds. These experiments demonstrated that the intensely bitter tastant denatonium induced a significant transient increase in [Ca²⁺]_i in cells transfected with one of the human candidate taste receptors, hT2R4, but not in control untransfected cells (Figure 3), or in cells transfected with other hT2Rs. The denatonium response had a strong dose-dependency with a threshold of ~100 μM. Interestingly, hT2R4 displayed a limited range of promiscuity since it also responded to high concentrations of the bitter tastant 6-n-propyl-2-thiouracil (PROP) (Figure 5).

If the responses of hT2R4 reflect the *in vivo* function of this receptor, it was hypothesized that similarly tuned receptors might be found in other species. The mouse receptor mT2R8 is a likely ortholog of hT2R4: they share ~70% identity, while the next closest receptor is only 40% identical; these two genes are contained in homologous genomic intervals. A rho-mT2R8 chimeric receptor was generated and examined for its response to a wide range of tastants. Indeed, mT2R8, like its human counterpart, is activated by denatonium and by high concentrations of PROP (Figures 3 and 5). No other tastants elicited significant responses from cells expressing mT2R8. Because these two receptors share only 70% identity, the similarity in their responses to bitter compounds attests to their role as orthologous bitter taste receptors.

Example VIII--Cycloheximide non-taster mice have mutations in the mT2R5 taste receptor

The demonstration that mT2R5 functions as a high affinity receptor for cycloheximide suggested that the mT2R5 gene might correspond to the Cyx locus. *In situ* hybridization to tissue sections demonstrated that the expression profile of mT2R5 is indistinguishable between taster and non-taster strains (Figure 6). To determine the linkage between mT2R5 and the Cyx locus, polymorphisms in the mT2R5 gene were identified and their distribution in a recombinant inbred panel from a C57BL/6J (non-taster) x DBA/2J (taster) cross was determined. Tight linkage was found between mT2R5 and the Cyx locus. To test the possibility that mutations in the mT2R5 gene were responsible for the Cyx phenotype, the mT2R5 gene was isolated from several additional well-characterized cycloheximide taster (CBA/Ca, BALB/c, C3H/He) and non-taster (129/Sv) strains and their nucleotide sequences determined. Indeed, as would be expected if mT2R5 functions as the cycloheximide receptor in these strains, all the tasters share the same mT2R5 allele as DBA/2J, while the non-tasters share the C57BL/6 allele, which carries missense mutations (Figure 6), including 3 non-conservative amino acid substitutions (T44I, G155D and L294R).

If the mT2R5 C57BL/6 allele is responsible for the taste deficiency of Cyx mutants, its cycloheximide dose-response might recapitulate the sensitivity shift seen in Cyx mutant strains. Two-bottle preference tests have shown that Cyx taster strains avoid cycloheximide with a threshold of 0.25 μ M, while non-tasters have a \sim 8-fold decrease in sensitivity (*e.g.* they, are non-tasters at 1 μ M, but strongly avoid cycloheximide at 8 μ M). A rho-mT2R5 fusion was constructed with the mT2R5 gene from a non-taster strain, and its dose response compared with that of the receptor from taster strains. Remarkably, mT2R5 from the non-taster strains displays a shift in cycloheximide sensitivity (Figure 4d) that resembles the sensitivity of these strains to this bitter tastant. Taken together, these results validate mT2R5 as a cycloheximide receptor, and strongly suggest that mT2R5 corresponds to the Cyx locus.

Example IX--T2Rs couple to gustducin

The above-described demonstration that T2Rs are co-expressed with gustducin suggests that T2Rs activate this G-protein in response to bitter tastants. To

investigate the selectivity of T2R - G-protein coupling, mT2R5 was chosen for study because its activation by cycloheximide recapitulates mouse taste responses. Rho-tagged mT2R5 and gustducin were prepared using a baculovirus expression system. mT2R5-containing membranes were incubated with various purified G-proteins, including

5 gustducin, and measured tastant-induced GTP- γ S binding (Hoon *et al.*, *Biochem J* 309:629-636 (1995)). Specifically, infectious Bacmid containing rhodopsin tagged mT2R5 (DBA/2-allele) was produced using the Bac-to-Bac system (Lifetechnologies, MD). Insect larval cells were infected for 60 h with recombinant Bacmid and membranes were prepared as described previously (Ryba and Tirindelli, *J Biol Chem*, 270:6757-6767

10 (1995)). Peripheral proteins were removed by treatment with 8 M urea and membranes were resuspended in 10 mM HEPES pH7.5, 1 mM EDTA and 1 mM DTT. The expression of rho-mT2R5 was assessed by Western blot using mAb B6-30 and quantitated by comparison with known amounts of rhodopsin. Approximately 300 pmol of rho-mT2R5 could be obtained from 2×10^8 infected cells. Gustducin and G $\beta_1\gamma_8$

15 heterodimers were isolated as described previously (Hoon *et al.*, *Biochem J* 309:629-636 (1995); Ryba and Tirindelli, *J Biol Chem*, 270:6757-6767 (1995)). Receptor-catalyzed exchange of GDP for GTP γ S on gustducin and other G-protein α -subunits was measured in the presence of 10 nM rho-mT2R5, 100 μ M GDP, and 20 μ M G $\beta_1\gamma_8$. All measurements were made at 15-minute time points, and reflect the initial rate of GTP γ S

20 binding.

These GTP- γ S binding assays revealed exquisite cycloheximide-dependent coupling of mT2R5 to gustducin (Figure 7). In contrast, no coupling was seen with G α_s , G α_i , G α_q or G α_o . No significant GTP γ S binding was observed in the absence of receptor, gustducin or $\beta\gamma$ -heterodimers. The high selectivity of T2R5 for gustducin, and

25 the exclusive expression of T2Rs in taste receptor cells that contain gustducin, affirm the hypothesis that T2Rs function as gustducin-linked taste receptors.

All publications and patent applications cited in this specification are

30 herein incorporated by reference as if each individual publication or patent application were specifically and individually indicated to be incorporated by reference.

Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be readily

SEQUENCE LISTING

SEQ ID NO:1

Human T2R01 amino acid sequence

5
MLESHLI IYFLLAVIQFLLGIFTNGIIVVNGIDLIKHRKMAPL D L L L SCLAVSRIFLQL
FIFYVNVIVIFFIEFIMCSANCAILLFINELELWLATWLGVFYCAKVASVRHPLFIWLKM
RISKLVPMILGSLLYVSMICVFHISKYAGFMVPYFLRKFFSQNATI QKEDTLAIQIFSFV
AEFSVPLLIIFLFAVLLLIIFSLGRHTRQMRNTVAGSRVPGRGAPISALLSILSFLILYFSH
10 CMIKVFLSSLKFHIRRFIFLFFILVIGIYPSGHSLLILILGNPKLKQNAKKFLLHSKCCQ

SEQ ID NO:2

Human T2R01 nucleotide sequence

15
ATGCTAGAGTCTCACCTCATTATCTATTTTCTTCTTGCAGTGATACAATTTCTTCTTGGG
ATTTTCACAAATGGCATCATTTGTGGTGGTGAATGGCATTGACTTGATCAAGCACAGAAAA
ATGGCTCCGCTGGATCTCCTTCTTTCTTGTCTGGCAGTTTCTAGAATTTTCTGCAGTTG
TTCATCTTCTACGTTAATGTGATTGTTATCTTCTTCATAGAATTCATCATGTGTTCTGCG
20 AATTGTGCAATTCTCTTATTTATAAATGAATTGGAAC TTTGGCTTGCCACATGGCTCGGC
GTTTTCTATTGTGCCAAGGTGGCAGCGTCCGTCACCCACTCTTCATCTGGTTGAAGATG
AGGATATCCAAGCTGGTCCCATGGATGATCCTGGGGTCTCTGCTATATGTATCTATGATT
TGTGTTTTCCATAGCAAATATGCAGGGTTTATGGTCCCATACTTCCTAAGGAAATTTTTC
TCCCAAATGCCACAATTCAAAAAGAAGATACACTGGCTATACAGATTTTCTCTTTTGT
25 GCTGAGTTCTCAGTGCCATTGCTTATCTTCCTTTTTGCTGTTTTGCTCTTGATTTTCTCT
CTGGGGAGGCACACCCGGCAAATGAGAAACACAGTGGCCGGCAGCAGGGTTCCTGGCAGG
GGTGCACCCATCAGCGCGTTGCTGTCTATCCTGTCCTTCCTGATCCTCTACTTCTCCAC
TGCATGATAAAAGTTTTTCTCTCTTCTCTAAAGTTTCACATCAGAAGGTTTCATCTTTCTG
TTCTTCATCCTTGTGATTGGTATATACCCTTCTGGACACTCTCTCATCTTAATTTTAGGA
30 AATCCTAAATTGAAACAAAATGCAAAAAGTTCTCCTCCAC**CAGTAAGTGCTGTCACTGA**

SEQ ID NO:3

Human T2R02 amino acid sequence

MALSFSAILHIIMMSAEFFTGITVNGFLIIVNCNELIKHRKLMPIQILLMCIGMSRFGLO
MVL MVQSFFSVFFPLLYVKIIYGAAMMFLWMFFSSISLWFATCLSVFYCLKISGFTQSCF
LWLKFRIPKLIPWLFWEAFWPL*ALHLCVEVDYAKNVEEDALRNTTLKKSKTKIKKISEV
5 LLVNLALIFPLAIFVMCTSMLLISLYKHTRMQHGSHGFRNANTEAHINALKTVITFFCF
FISYFAAFMTNMTFSLPYRSHQFFMLKDIMAAYPSGHSVIIILSNSKFQQSFRRILCLKK
KL

10 **SEQ ID NO:4**

Human T2R02 nucleotide sequence

ATGGCCTTGTCCTTTTTCAGCTATTCTTCATATTATCATGATGTCAGCAGAATTCTTCACA
GGGATCACAGTAAATGGATTTCCTTATCATTGTTAACTGTAATGAATTGATCAAACATAGA
15 AAGCTAATGCCAATTCAAATCCTCTTAATGTGCATAGGGATGTCTAGATTGTTGGTCTGCAG
ATGGTGTTAATGGTACAAAGTTTTTCTCTGTGTTCTTTCCACTCCTTTACGTCAAATA
ATTTATGGTGCAGCAATGATGTTCTTTGGATGTTTTTTAGCTCTATCAGCCTATGGTTT
GCCACTTGCCCTTCTGTATTTTACTGCCTCAAGATTTTCAGGCTTCACTCAGTCCTGTTTT
CTTTGGTTGAAATTCAGGATCCCAAAGTTAATACCTTGGCTGCTTCTGGGAAGCGTTCTG
20 GCCTCTGTGAGCATTGCATCTGTGTGTCGAGGTAGATTACGCTAAAAATGTGGAAGAGGA
TGCCCTCAGAAACACCACACTAAAAAAGAGTAAACAAAGATAAAGAAAATTAGTGAAGT
GCTTCTTGTCAACTTGGCATTAAATATTTCTCTAGCCATATTTGTGATGTGCACTTCTAT
GTTACTCATCTCTCTTTACAAGCACACTCATCGGATGCAACATGGATCTCATGGCTTTAG
AAATGCCAACACAGAAGCCCATATAAATGCATTAAAAACAGTGATAACATTCTTTTGCTT
25 CTTTATTTCTTATTTTGCTGCCTTCATGACAAATATGACATTTAGTTTACCTTACAGAAG
TCACCAGTTCTTTATGCTGAAGGACATAATGGCAGCATATCCCTCTGGCCACTCGGTTAT
AATAATCTTGAGTAATTCTAAGTTCCAACAATCATTTAGAAGAATTCTCT**GCTCAAAAA**
GAAACTATGA

30

SEQ ID NO:5

Human T2R03 amino acid sequence

MMGLTEGVFLILSGTQFTLGILVNCFIELVNGSSWFKTKRMSLSDFIITTLALLRIILLC
 IILTDSFLIEFSPNTHDSGIIMQIIDVSWTFTNHLSIWLATCLGVLYCLKIASFSHPTFL
 WLKWRVSRVMVWMLLGALLSCGSTASLINEFKLYSVFRGIEATRNVTEHFRKKRSEYYL
 IHVLGTLWYLPPLIVSLASYSLIFSLGRHTRQMLQNGTSSRDPTTEAHKRAIRIILSFF
 5 FLFLLYFLAFLIASFGNFLPKTKMAKMIGEVMTMFY PAGHSFILILGNSKLKQTFVVMLR
 CESGHLKPGSKGPIFS

SEQ ID NO:6

10 Human T2R03 nucleotide sequence

ATGATGGGACTCACCGAGGGGGTGTTCCTGATTCTGTCTGGCACTCAGTTCACACTGGGA
 ATTCTGGTCAATTGTTTCATTGAGTTGGTCAATGGTAGCAGCTGGTTCAAGACCAAGAGA
 ATGTCTTTGTCTGACTTCATCATCACCACCCTGGCACTCTTGAGGATCATTCTGCTGTGT
 15 ATTATCTTGACTGATAGTTTTTTAATAGAATTCTCTCCCAACACACATGATTCAGGGATA
 ATAATGCAAATTATTGATGTTTCCTGGACATTTACAAACCATCTGAGCATTGGCTTGCC
 ACCTGTCTTGGTGTCTCTACTGCCTGAAAATCGCCAGTTTCTCTCACCCACATTCCTC
 TGGCTCAAGTGGAGAGTTTCTAGGGTGATGGTATGGATGCTGTTGGGTGCACTGCTCTTA
 TCCTGTGGTAGTACCGCATCTCTGATCAATGAGTTTAAGCTCTATTCTGTCTTTAGGGGA
 20 ATTGAGGCCACCAGGAATGTGACTGAACACTTCAGAAAGAAGAGGAGTGAGTATTATCTG
 ATCCATGTTCTTGGGACTCTGTGGTACCTGCCTCCCTTAATTGTGTCCCTGGCCTCCTAC
 TCTTTGCTCATCTTCTCCCTGGGGAGGCACACACGGCAGATGCTGCAAAATGGGACAAGC
 TCCAGAGATCCAACCACTGAGGCCCACAAGAGGGCCATCAGAATCATCCTTTCCTTCTTC
 TTTCTCTTCTTACTTTACTTTCTTGCTTTCTTAATTGCATCATTTGGTAATTTCTACCA
 25 AAAACCAAGATGGCTAAGATGATTGGCGAAGTAATGACAATGTTTTATCCTGCTGGCCAC
 TCATTTATTCTCATTCTGGGGAACAGTAAGCTGAAGCAGACATTTGTAGTGATGCTCCGG
 TGTGAGTCTGGTCATCTGAAGCCTGGATCCA**AGGGACCCATTTTCTCTTAG**

SEQ ID NO:7

Human T2R04 amino acid sequence

MLRLFYFSIIASVILNFVGIIMNLFITVFNCKTWVKSHRISSSDRILFSLGITRFLMLG
 LFLVNTIYFVSSNTERSVYLSAFFVLCFMFLDSSSVWFVTLNILYCVKITNFQHSVFL

LKRNISPKIPRLLLACVLISAFTTCLYITLSQASPFPELVTRNNTSFNISEGILSLVVS
LVLSSSLQFIINVTSASLLIHSLRRHIQKMQKNATGFWNPQTEAHVGAMKLMVYFLILYI
PYSVATLVQYLPFYAGMDMGTKSICLIFATLYSPGHSVLIIITHPKLKTTAKKILCFKK

5

SEQ ID NO:8

Human T2R04 nucleotide sequence

ATGCTTCGGTTATTCTATTTCTCTGCTATTATTGCCTCAGTTATTTTAAATTTTGTAGGA
10 ATCATTATGAATCTGTTTATTACAGTGGTCAATTGCAAACTTGGGTCAAAAGCCATAGA
ATCTCCTCTTCTGATAGGATTCTGTTCAGCCTGGGCATCACCAGGTTTCTTATGCTGGGA
CTATTTCTGGTGAACACCATCTACTTCGTCTCTTCAAATACGGAAAGGTCAGTCTACCTG
TCTGCTTTTTTTGTGTTGTGTTTCATGTTTTTGGACTCGAGCAGTGTCTGGTTTGTGACC
TTGCTCAATATCTTGTACTGTGTGAAGATTACTAACTTCCAACACTCAGTGTTTCTCCTG
15 CTGAAGCGGAATATCTCCCCAAAGATCCCCAGGCTGCTGCTGGCCTGTGTGCTGATTTCT
GCTTTCACCACTTGCCTGTACATCAGCTTAGCCAGGCATCACCTTTTCCTGAACTTGTG
ACTACGAGAAATAACACATCATTTAATATCAGTGAGGGCATCTTGTCTTTAGTGGTTTCT
TTGGTCTTGAGCTCATCTCTCCAGTTCATCATTAATGTGACTTCTGCTTCCTTGCTAATA
CACTCCTTGAGGAGACATATACAGAAGATGCAGAAAAATGCCACTGGTTTCTGGAATCCC
20 CAGACGGAAGCTCATGTAGGTGCTATGAAGCTGATGGTCTATTTCCCTCATCCTCTACATT
CCATATTCAGTTGCTACCCTGGTCCAGTATCTCCCCTTTTATGCAGGGATGGATATGGGG
ACCAAATCCATTTGTCTGATTTTTGCCACCCTTTACTCTCCAGGACATTCTGTTCTCATT
ATTATCACACATCCTAAACTGAAAACAACAGCAAA**GAAGATTCTTTGTTTCAAAAATAG**

25

SEQ ID NO:9

Human T2R05 amino acid sequence

MLSAGLGLMLVAVVEFLIGLIGNGLVVWSFREWIRKFNWSSYNLIILGLAGCRFLLQW
30 LIILDLSLFPLFQSSRWLRYLSIFWVLVSQASLWFATFLSVFYCKKITTFDRPAYLWLKQ
RAYNLSLWCLLGYFIINLLLTVQIGLTFYHPPQGNSSIRYPFESWQYLYAFQLNSGSYLP
LVVFLVSSGMLIVSLYTHHKMKVHSAGRRDVRAKAHITALKSLGCFLLHLVYIMASPF
SITSKTYPPDLTSVFIWETLMAAYPSLHSLILIMGIPRVKQTCQKILWKTVCARRCWGP

SEQ ID NO:10

Human T2R05 nucleotide sequence

5 **ATGCTGAGCGCTGGCCTAG** GACTGCTGATGCTGGTGGCAGTGGTTGAATTTCTCATCGGT
TTAATTGGAAATGGAAGCCTGGTGGTCTGGAGTTTTAGAGAATGGATCAGAAAATTCAAC
TGGTCCTCATATAACCTCATTATCCTGGGCCTGGCTGGCTGCCGATTTCTCCTGCAGTGG
CTGATCATTTTGGACTTAAGCTTGTTTCCACTTTTCCAGAGCAGCCGTTGGCTTCGCTAT
CTTAGTATCTTCTGGGTCCTGGTAAGCCAGGCCAGCTTATGGTTTGCCACCTTCCTCAGT
10 GTCTTCTATTGCAAGAAGATCACGACCTTCGATCGCCCGGCCTACTTGTGGCTGAAGCAG
AGGGCCTATAACCTGAGTCTCTGGTGCCTTCTGGGCTACTTTATAATCAATTTGTTACTT
ACAGTCCAAATTGGCTTAACATTCTATCATCCTCCCCAAGGAAACAGCAGCATTCGGTAT
CCCTTTGAAAGCTGGCAGTACCTGTATGCATTTACAGCTCAATTCAGGAAGTTATTTGCCT
TTAGTGGTGTTTCTTGTTTCCCTCTGGGATGCTGATTGTCTCTTTGTATACACACCACAAG
15 AAGATGAAGGTCCATTACAGCTGGTAGGAGGGATGTCCGGGCCAAGGCTCACATCACTGCG
CTGAAGTCCTTGGGCTGCTTCCTCTTACTTCACCTGGTTTATATCATGGCCAGCCCCCTTC
TCCATCACCTCCAAGACTTATCCTCCTGATCTCACCAGTGTCTTCATCTGGGAGACACTC
ATGGCAGCCTATCCTTCTCTTCATTCTCTCATATTGATCATGGGGATTCTAGGGTGAAG
CAGACTTGTCAGAAGATCCTGTGGAAGACAGTGTGTGCTCG**GAGATGCTGGGGCCCATGA**

20

SEQ ID NO:11

Human T2R06 amino acid sequence

25 MLAAALGLLMPIAGAEFLIGLVNGVPVVC SFRGWVKM*GVPINSHDSGK*PLSPTQAD
HVGHKSVSTFPEQWLALLS*CLRVLV SQANM*FATFFSGFCCMEIMTFVXXXXXXXXXXXXX
XXXXXXXXXXLLVSFKITFYFSALVGWTL*KPLTGNSNILHPILNLLFL*IAVQ*RRLIAI
CDVSVPLVFL*RHHRKMEDHTAVRRRLKPRXXXXXXXXXXXXXXXXXXLYMVSALARHFSMTF
*SPSDLTILAISATLMAVYTSFPSIVMVMRNQTCQRIL*EMICTWKS

30

SEQ ID NO:12

Human T2R06 nucleotide sequence

ATGTTGGCGGCTGCCCTAGGATTGCTGATGCCCATTCAGGGGCTGAATTTCTCATTGGC
 CTGGTTGGAAATGGAGTCCCTGTGGTCTGCAGTTTTAGAGGATGGGTCAAAAAAATGTAA
 GGAGTCCCTATAAATTCTCATGATTCTGGTAAGTAGCCACTTTCTCCTACTCAGGCCGAT
 CATGTTGGACATAAGTCTGTTTCCACTTTCCCAGAGCAGTGGTTGGCTTTACTATCTTAA
 5 TGTCTTCGAGTCCTGGTAAGCCAGGCCAACATGTAGTTTGCCACTTTCTTCAGTGGCTTC
 TGCTGCATGGAGATCATGACCTTTGTCCCGCTGACTTCTTGTAGCTGAAAAGACTGGGTT
 TTTGTTTTTTTGCTAGTGTCTTTCAAGATCACTTTTTATTTCTCAGCTCTTGTGGCTGGA
 CCCTTTAAAACCCTTAACAGGAAACAGCAACATCCTGCATCCCATTTTAAATCTGTTAT
 TTTTATAGATTGCTGTCCAGTGAAGGAGACTGATTGCTATTTGTGATGTTTCTGTTCCAC
 10 TTGTCTTTTTGTAAAGACATCACAGGAAGATGGAGGACCACACAGCTGTCAGGAGGAGGC
 TCAAACCAAGGTGCTCATCGCTCTGAACCTCCCCCTTACATGGTTTCTGCCTTGCCAG
 ACACTTTTCCATGACCTTCTAATCTCCCTCTGATCTCACCATTCTTGCCATCTCTGCAAC
 ACTCATGGCTGTTTATACTTCATTTCCGTCTATTGTAATGGTTATGAGGAATCAGACTTG
 TCAGAGAATTCTGTAGGAGATGATATGTACATGGAAATCCTAG

15

SEQ ID NO:13

Human T2R07 amino acid sequence

20 MADKVQTTLLFLAVGEFSVGILGNAFIGLVNCDWVKKRKIASIDLILTSLAISRICLLC
 VILLDCFILVLYPDVYATGKEMRIIDFFWTLTNHLSIWFATCLSIYYFFKIGNFFHPLFL
 WMKWRIDRVISWILLGCVVLSVFISLPATENLNADFRFCVKAKRKTNLTWSCRVNKTQHA
 STKLFLNLATLLPFCVCLMSFFLLILSLRRHIRRMQLSATGCRDPSTEAHVRALKAVISF
 LLLFIAYYLSFLIATSSYFMPETELAVIFGESIALIYPSSHFILILGNKLRHASLKVI
 25 WKVMSILKGRKFQQHKQI

SEQ ID NO:14

Human T2R07 nucleotide sequence

30

ATGGCAGATAAAGTGCAGACTACTTTTATTGTTCTTAGCAGTTGGAGAGTTTTTCAGTGGGG
 ATCTTAGGGAATGCATTCATTGGATTGGTAAACTGCATGGACTGGGTCAAGAAGAGGAAA
 ATTGCCTCCATTGATTTAATCCTCACAAGTCTGGCCATATCCAGAATTTGTCTATTGTGC
 GTAATACTATTAGATTGTTTTATATTGGTGCTATATCCAGATGTCTATGCCACTGGTAAA

GAAATGAGAATCATTGACTTCTTCTGGACACTAACCAATCATTTAAGTATCTGGTTTGCA
ACCTGCCTCAGCATTTACTATTTCTTCAAGATAGGTAATTTCTTTCACCCACTTTTCCTC
TGGATGAAGTGGAGAATTGACAGGGTGATTTCTGGATTCTACTGGGGTGCGTGGTTCTC
TCTGTGTTTATTAGCCTTCCAGCCACTGAGAATTTGAACGCTGATTTTCAGGTTTTGTGTG
5 AAGGCAAAGAGGAAAACAACTTAACTTGGAGTTGCAGAGTAAATAAACTCAACATGCT
TCTACCAAGTTATTTCTCAACCTGGCAACGCTGCTCCCCTTTTGTGTGTGCCTAATGTCC
TTTTTCCTCTTGATCCTCTCCCTGCGGAGACATATCAGGCGAATGCAGCTCAGTGCCACA
GGGTGCAGAGACCCCAGCACAGAAGCCCATGTGAGAGCCCTGAAAGCTGTCATTTCCCTTC
CTTCTCCTCTTTATTGCCTACTATTTGTCCTTTCTCATTGCCACCTCCAGCTACTTTATG
10 CCAGAGACGGAATTAGCTGTGATTTTTGGTGAGTCCATAGCTCTAATCTACCCCTCAAGT
CATTCATTTATCCTAATACTGGGGAACAATAAATTAAGACATGCATCTCTAAAGGTGATT
TGGAAAGTAATGTCTATTCTAAAAGGAAGAAAATT**CCAACAACATAAACAATCTGA**

15 **SEQ ID NO:15**

Human T2R08 amino acid sequence

MFSPADNIFIILITGEFILGILGNGYIALVNWIDWIKKKKISTVDYILTNLVIARICLIS
VMVNGIVIVLNPDVYTKNKQQIVIFTFWTFANYLNMWITTCLNVFYFLKIASSSHPLFL
20 WLKWKIDMVVHWILLGCF AISLLVSLIAAIVLSCDYRFHAI AKHKRNITEMFHVSKIPIFY
EPLTLFNLFAIVPFIIVSLISFLLVRS LWRHTKQIKLYATGSRDPSTEVHVRAIKTMTSF
IFFFFLYYISSILMTFSYLMTKYKLAVEFGEIAAILYPLGHS LILIVLNNKLRQTFVRML
TCRKIACMI

25

SEQ ID NO:16

Human T2R08 nucleotide sequence

ATGTT CAGT CCTGCAGATAACATCTTTATAATCCTAATAACTGGAGAATTCATACTAGGA
30 ATATTGGGGAATGGATACATTGCACTAGTCAACTGGATTGACTGGATTAAAGAAGAAAAAG
ATTTCCACAGTTGACTACATCCTTACCAATTTAGTTATCGCCAGAATTTGTTTGATCAGT
GTAATGGTTGTAAATGGCATTGTAATAGTACTGAACCCAGATGTTTATACAAAAAATAAA
CAACAGATAGTCATTTTTACCTTCTGGACATTTGCCAACTACTTAAATATGTGGATTACC
ACCTGCCTTAATGTCTTCTATTTTCTGAAGATAGCCAGTTCCTCTCATCCACTTTTTCTC

TGGCTGAAGTGGAAAATTGATATGGTGGTGCACCTGGATCCTGCTGGGATGCTTTGCCATT
 TCCTTGTTGGTCAGCCTTATAGCAGCAATAGTACTGAGTTGTGATTATAGGTTTCATGCA
 ATTGCCAAACATAAAAGAAACATTACTGAAATGTTCCATGTGAGTAAAATACCATACTTT
 GAACCCTTGACTCTCTTTAACCTGTTTGCAATTGTCCCATTTATTGTGTCACTGATATCA
 5 TTTTTCCTTTTAGTAAGATCTTTATGGAGACATACCAAGCAAATAAACTCTATGCTACC
 GGCAGTAGAGACCCCAGCACAGAAGTTCATGTGAGAGCCATTAAACTATGACTTCATTT
 ATCTTCTTTTTTTTCTATACTATATTTCTTCTATTTTGATGACCTTTAGCTATCTTATG
 ACAAATAACAAGTTAGCTGTGGAGTTTGGAGAGATTGCAGCAATTCTCTACCCCTTGGGT
 CACTCACTTATTTTAATTGTTTTAAATAATAAACTGAGGCAGACATTTGTCAGAATGCTG
 10 ACATGTAGAAAAATTGCCTGCATGATATGA

SEQ ID NO:17

Human T2R09 amino acid sequence

15 MPSAIEAIYIILIAGELTIGIWGNFIVLVNCIDWLKRRDISLIDIILISLAISRICLLC
 VISLDGFFMLLPFGTYGNSVLVSIVNVVWTFANNSSLWFTSCLSIFYLLKIANISHPFFF
 WLKLKINKVMLAILLGSFLISLIISVPKNDDMWYHLFKVSHEENITWKFKVSKIPIGTFKQ
 LTLNLGVMVPFILCLISFFLLLFSLVRHTKQIRLHATGFRDPSTEAHMRAIKAVIIFLLL
 20 LIVYYPVFLVMTSSALIPQGLVLMIGDIVTVIFPSSHFILIMGNSKLR AFLKMLRFV
 KCFLRRRKPFVP

SEQ ID NO:18

25 Human T2R09 nucleotide sequence

ATGCCAAGTGCAATAGAGGCAATATATATTATTTTAATTGCTGGTGAATTGACCATAGGG
 ATTTGGGGAAATGGATTCATTGTACTAGTTAACTGCATTGACTGGCTCAAAGAAGAGAT
 ATTTCTTGATTGACATCATCCTGATCAGCTTGGCCATCTCCAGAATCTGTCTGCTGTGT
 30 GTAATATCATTAGATGGCTTCTTTATGCTGCTCTTCCAGGTACATATGGCAATAGCGTG
 CTAGTAAGCATTGTGAATGTTGTCTGGACATTTGCCAATAATTCAAGTCTCTGGTTTACT
 TCTTGCCTCAGTATCTTCTATTTACTCAAGATAGCCAATATATCGCACCCATTTTCTTC
 TGGCTGAAGCTAAAGATCAACAAGGTCATGCTTGCATTCTTCTGGGGTCCTTTCTTATC
 TCTTTAATTATTAGTGTTCCAAAGAATGATGATATGTGGTATCACCTTTTCAAAGTCAGT

CATGAAGAAAACATTACTTGGAATTCAAAGTGAGTAAAATTCCAGGTACTTTCAAACAG
 TTAACCCTGAACCTGGGGGTGATGGTTCCCTTTATCCTTTGCCTGATCTCATTCTTTCTTG
 TTACTTTTCTCCCTAGTTAGACACACCAAGCAGATTGCGACTGCATGCTACAGGGTTCAGA
 GACCCCAGTACAGAGGCCACATGAGGGCCATAAAGGCAGTGATCATCTTTCTGCTCCTC
 5 CTCATCGTGTACTACCCAGTCTTTCTTGTTATGACCTCTAGCGCTCTGATTCTCAGGGA
 AAATTAGTGTGATGATTGGTGACATAGTAAGTGTCAATTTCCCATCAAGCCATTCATTC
 ATTCTAATTATGGGAAATAGCAAGTTGAGGGAAGCTTTTCTGAAGATGTTAAGATTTGTG
 AAGTGTTTCCTTAGAAGAAG**GAAAGCCTTTTGTTCCATAG**

10

SEQ ID NO:19

Human T2R10 amino acid sequence

MLRVVEGIFIFVVVSESVFGVLGNFIGLVNCIDCAKNKLSTIGFILTGLAISRIFLIWI
 15 IITDGFIIQIFSPNIYASGNLIEYISYFWVIGNQSSMWFATSLSIFYFLKIANFSNYIFLW
 LKSRTNMVLPFMIVFLLISSLLNFAYIAKILNDYKTKNDTVWDLNMYKSEYFIKQILLNL
 GVIFFFTLSLITCIFIILSLWRHNRQMOSNVTGLRDSNTEAHVKAMKVLISFIILFIFYF
 IGMAIEISCFTVRENKLLLMFGMTTTAIYPWGHSFILILGNSKLKQASLRVLQQLKCEK
 RKNLRVT

20

SEQ ID NO:20

Human T2R10 nucleotide sequence

25 **ATGCTACGTGTAGTGGAAG**GCATCTTCATTTTTGTTGTAGTTAGTGAGTCAGTGTTTGGG
 GTTTTGGGGAATGGATTTATTGGACTTGTAAGTGCATTGACTGTGCCAAGAATAAGTTA
 TCTACGATTGGCTTTATTCTCACCGGCTTAGCTATTTCAAGAATTTTTCTGATATGGATA
 ATAATTACAGATGGATTTATACAGATATTCTCTCAAATATATATGCCTCCGGTAACCTA
 ATTGAATATATTAGTTACTTTTGGGTAATTGGTAATCAATCAAGTATGTGGTTTGCCACC
 30 AGCCTCAGCATCTTCTATTTCTGAAGATAGCAAATTTTTCCAACATACATTTTCTCTGG
 TTGAAGAGCAGAACAAATATGGTTCTTCCCTTCATGATAGTATTCTTACTTATTTTCATCG
 TTAATTTTGCATACATTGCGAAGATTCTTAATGATTATAAAACGAAGAATGACACA
 GTCTGGGATCTCAACATGTATAAAGTGAATACTTTATTAAACAGATTTTGCTAAATCTG
 GGAGTCATTTTCTTCTTTACACTATCCCTAATTACATGTATTTTTTTAATCATTTCCCTT

TGGAGACACAACAGGCAGATGCAATCGAATGTGACAGGATTGAGAGACTCCAACACAGAA
 GCTCATGTGAAGGCAATGAAAGTTTTGATATCTTTCATCATCCTCTTTATCTTGTATTTT
 ATAGGCATGGCCATAGAAATATCATGTTTTACTGTGCGAGAAAACAACTGCTGCTTATG
 TTTGGAATGACAACCACAGCCATCTATCCCTGGGGTCACTCATTTATCTTAATTCTAGGA
 5 AACAGCAAGCTAAAGCAAGCCTCTTTGAGGGTACTGCAGCAATTGAAGTGCTGTGAGAAA
AGGAAAAATCTCAGAGTCACATAG

SEQ ID NO:21

10 Human T2R11 amino acid sequence

MANMLKNMLTMISAIIDFIMGIQSRVMVLVHCIDWIRRWKLSLIDFILTCWAISRIFFXX
 XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXNHLCT*FATCLAVFYFLKIVNFSYLFYFWLK
 WRINKVAFILPLVSAFSVYQLSFDVHF*CLLVSCPKEYERHMTGLLNVSNNKNVNNIIIF
 15 FIGSLSSFSISSIFFLLLLLSS*RHMKHIRENFRDCRTPVYGPISEPRKRESFFVLLLYK
 NLPFS

SEQ ID NO:22

20 Human T2R12 amino acid sequence

MSSIWETLFIRILVV*FIMGTVGN*FIVLVNIID*IRN*KVSLIDFILNCLAISRICFL*
 ITILATSFNIGYEKMPDSKNLAVSFDILWTGSSYFCLSCCTTCLSVFYFLKIVANFSNPIFL
 WMKWKIHKVLLFIVLEATISFCTTSILKEIINSILI*ERVTIKGNLTFNYMDTMHDFTS
 25 FLLQMMFILPFVETLASILLILSLWSHTRQMKLHGIYSRDPSTEAHVKPIKAIISFLLL
 FIVHYFISIIILTLACPLLDVFAARTFSSVLVFFHPSGHSFLLILRDSKLKQASLCVLKKM
 KYAKKDIISHFYKHA

30 **SEQ ID NO:23**

Human T2R12 nucleotide sequence

ATGTCAAGCATTGGGGAGACACTGTTTATAAGAATTCTTGTAGTGTAATTCATAATGGGG
 ACTGTGGGAAATTGATTCATTGTATTGGTTAATATCATTGACTGAATCAGGAACTGAAAG

GTCTCCCTGATTGATTTTATTCTCAACTGCTTGGCCATCTCCAGGATATGTTTCCTGTAG
ATAACAATTTTAGCTACCTCTTTCAATATAGGCTATGAGAAAATGCCTGATTCTAAGAAT
CTTGACAGTAAGTTTTGACATTCTCTGGACAGGATCCAGCTATTTCTGCCTGTCCTGTACC
ACTTGCCTCAGTGTCTTCTATTTCTCAAGGTAGCCAACTTCTCCAATCCCATTTTCCTC
5 TGGATGAAATGGAAAATTCACAAGGTGCTTCTCTTTATTGTAAGGCAACGATCTCT
TTCTGCACAACTTCCATTCTGAAGGAAATAATAATTAATAGTTTAATCTAAGAACGGGTA
ACAATAAAAGGCAACTTGACATTTAATTATATGGATACCATGCATGATTTCACTTCTCTG
TTTCTCCTTC**AG**ATGATGTTTCATCCTTCCTTTTGTGGAAACACTGGCTTCCATTCTTCTC
TTAATCCTCTCCTTATGGAGCCACACCAGGCAGATGAAGCTACATGGTATTTATTCCAGG
10 GATCCCAGCACAGAAGCCCATGTAAACCTATAAAAGCTATAATTTCAATTTCTACTCCTC
TTTATTGTGCATTATTTTCATCAGTATCATACTAACATTGGCCTGTCCTCTTCTAGACTTC
GTTGCGGCAAGGACTTTTAGTAGTGTGCTGGTATTTTTCCATCCATCTGGCCATTCATTT
CTTCTAATTTTACGGGACAGCAAACCTGAAGCAAGCTTCTCTCTGTGTCCTGAAGAAGATG
AAGTATGCCAAAAGGACATAATCT**CTCATTTTTATAAACATGCCTGA**

15

SEQ ID NO:24

Human T2R13 amino acid sequence

20 MESALPSIFTLVIIAEFIIGNLSNGFIVLINCIDWVSKRELSSVDKLLIILAISRIGLIW
EILVSWFLALHYLAIFVSGTGLRIMIFSWIVSNHFNWLATIFSIFYLLKIASFSSPAFL
YLKWRVNVKILMILLGTLVFLFLNLIQINMHIKDWLDRYERNTTNWFSMSDFETFSVSVK
FTMTMFSLTPFTVAFISFLLLIIFSLQKHLQKMLNYKGHRDPRTKVHTNALKIVISFLLF
YASFFLCVLISWISELYQNTVIYMLCETIGVFSPSSHFLILGNAKLRLQAFLLVAAKVW
25 AKR

SEQ ID NO:25

Human T2R13 nucleotide sequence

30

ATGGAAAGTGCCCTGCCGAGTATCTTCACTCTTGTAATAATTGCAGAATTCATAATTGGG
AATTTGAGCAATGGATTTATAGTACTGATCAACTGCATTGACTGGGTCAGTAAAAGAGAG
CTGTCCTCAGTCGATAAACTCCTCATTATCTTGGCAATCTCCAGAATTGGGCTGATCTGG
GAAATATTAGTAAGTTGGTTTTAGCTCTGCATTATCTAGCCATATTTGTGTCTGGAACA

GGATTAAGAATTATGATTTTTAGCTGGATAGTTTCTAATCACTTCAATCTCTGGCTTGCT
 ACAATCTTCAGCATCTTTTATTTGCTCAAAATAGCGAGTTTCTCTAGCCCTGCTTTTCTC
 TATTTGAAGTGGAGAGTAAACAAAGTGATTCTGATGATACTGCTAGGAACCTTGGTCTTC
 TTATTTTTAAATCTGATACAAATAAACATGCATATAAAAGACTGGCTGGACCGATATGAA
 5 AGAAACACAACCTTGAATTTTCAGTATGAGTGACTTTGAAACATTTTCAGTGTCGGTCAA
 TTCATATGACTATGTTTCAGTCTAACACCATTTACTGTGGCCTTCATCTCTTTTCTCCTG
 TTAATTTTCTCCCTGCAGAAACATCTCCAGAAAATGCAACTCAATTACAAAGGACACAGA
 GACCCCAGGACCAAGGTCCATACAAATGCCTTGAAAATTGTGATCTCATTCTTTTATTC
 TATGCTAGTTTCTTTCTATGTGTTCTCATATCATGGATTTCTGAGCTGTATCAGAACACA
 10 GTGATCTACATGCTTTGTGAGACGATTGGAGTCTTCTCTCCTTCAAGCCACTCCTTTCTT
 CTGATTCTAGGAAACGCTAAGTTAAGACAGGCCTTTCTTTTGGTGGCAGCTAAGGTATGG
GCTAAACGATGA

15 **SEQ ID NO:26**

Human T2R14 amino acid sequence

MGGVIKSIFTFVLIVEFIIGNLGNSFIALVNCIDWVKGRKISSVDRILTALAISRI¹SLVW
 LIFGSWCVSVFFPALFATEKMFRMLTNIWTVINHFSVWLATGLGTFYFLKIANFNSN²IFL
 20 YLKWRVKKVVLVLLLVT³SVFLFLNIALINIHINASINGYRRNKTCSSDSSNFTRESSLIV
 LTSTVFIFIFPFTLSLAMFLLLI⁴FSMWKHRKKMQHTVKISGDASTKAHRGVKSVITFFLLY
 AIFSL⁵SFFISVWTSERLEENLIILSQVMGMAYPSCHSCVLILGNKKLRQASLSVLLWLRY
 MFKDGEPSGHKEFRESS

25

SEQ ID NO:27

Human T2R14 nucleotide sequence

ATGGGTGGTGTCATAAAGAGCATATTTACATTCGTTTTAATTGTGGAATTTATAATTGGA
 30 AATTTAGGAAATAGTTTCATAGCACTGGTGAAGTGTATTGACTGGGTCAAGGGAAGAAAG
 ATCTCTTCGGTTGATCGGATCCTCACTGCTTTGGCAATCTCTCGAATTAGCCTGGTTTGG
 TTAATATTCGGAAGCTGGTGTGTGTCTGTGTTTTTCCCAGCTTTATTTGCCACTGAAAAA
 ATGTT⁶CAGAATGCTTACTAATATCTGGACAGTGATCAATCATTTTAGTGTCTGGTTAGCT
 ACAGGCCTCGGTACTTTTTATTTTCTCAAGATAGCCAATTTTCTAACTCTATTTTCTC

TACCTAAAGTGGAGGGTTAAAAAGGTGGTTTTTGGTGCTGCTTCTTGTGACTTCGGTCTTC
 TTGTTTTTAAATATTGCACTGATAAACATCCATATAAATGCCAGTATCAATGGATACAGA
 AGAAACAAGACTTGCACTTCTGATTCAAGTAACCTTTACACGATTTTCCAGTCTTATTGTA
 TTAACCAGCACTGTGTTTCATTTTCATACCCTTTACTTTGTCCCTGGCAATGTTTCTTCTC
 5 CTCATCTTCTCCATGTGGAAACATCGCAAGAAGATGCAGCACACTGTCAAAATATCCGGA
 GAGCCAGCACCAAAGCCCACAGAGGAGTTAAAAGTGTGATCACTTTCTTCCCTACTCTAT
 GCCATTTTCTCTCTGTCTTTTTTCATATCAGTTTGGACCTCTGAAAGGTGGAGGAAAAT
 CTAATTATTCTTTCCCAGGTGATGGGAATGGCTTATCCTTCATGTCACTCATGTGTTCTG
 ATTCTTGGAAACAAGAAGCTGAGACAGGCCTCTCTGTCTAGTGCTACTGTGGCTGAGGTAC
 10 ATGTTCAAAGATGGGGAGCCCTCAGGTCACAAAG**GAATTTAGAGAATCATCTTGA**

SEQ ID NO:28

Human T2R15 amino acid sequence

15 MITFLPIIFSILVVVTFVLGNFANGFIVLVNSIEWVKRQKISFADQILTALAVSRVGLLW
 VILLHWYATVLNPGSYSLSLGVRIITINAWAVTNHFSIWWATSLSIFYFLKIANFSNFIFLH
 LKRRIKSVIPVILLGSLFLVCHLVVVNMDESMWTKEYEGNVSWEIKLSDPHLSDMTVT
 TLANLIPFTLSLLSFLLLICSLCKHLKMQFHGKGSPDSNTKVHIKALQTVTSFLLLFAV
 20 YFLSLITSIWNFRRL*NEPVLMLSQTTAIIYPSFHSFILIWGSKKLKQTFLLILCQIKC

SEQ ID NO:29

Human T2R15 nucleotide sequence

25 **ATGATAACTTTTCTACCCATCATTTTTTCCATTCTAGTAGTGGTTACATTTGTTCTTGGG**
 AATTTTGCTAATGGCTTCATAGTGTTGGTAAATTCATTGAGTGGGTCAAGAGACAAAAG
 ATCTCCTTTGCTGACCAAATTCTCACTGCTCTGGCAGTCTCCAGAGTTGGTTTGCTCTGG
 GTAATATTATTACATTGGTATGCAACTGTTTTGAATCCAGGTTCAATAGTTTAGGAGTA
 30 AGAATTACTACTATTAATGCCTGGGCTGTAACCAACCATTTAGCATCTGGGTTGCTACT
 AGCCTCAGCATATTTTATTTCTCAAGATTGCCAATTTCTCCAACCTTTATTTTTCTTCAC
 TTAAAAGGAGAATTAAGAGTGTCATTCCAGTGATACTATTGGGGTCTTTGTTATTTTTG
 GTTTGTCATCTTGTGTTGTGGTAAACATGGATGAGAGTATGTGGACAAAAGAATATGAAGGA
 AACGTGAGTTGGGAGATCAAATTGAGTGATCCGACGCACCTTTCAGATATGACTGTAACC

ACGCTTGCAAACCTTAATACCCTTTACTCTGTCCCTGTTATCTTTTCTGCTCTTAATCTGT
TCTTTGTGTAAACATCTCAAGAAGATGCAGTTCCATGGCAAAGGATCTCCAGATTCCAAC
ACCAAGGTCCACATAAAAGCTTTGCAAACGGTGACCTCCTTCCTCTTGTTATTTGCTGTT
TACTTTCTGTCCCTAATCACATCGATTTGGAATTTTAGGAGGAGGCTGTAGAACGAACCT
5 GTCCTCATGCTCAGCCAACTACTGCAATTATATAACCCTTCATTTCAATTCATTCATCCTA
ATTTGGGGAAGCAAGAAGCTGAAACAGACCTTCTTTTGATTTT**GTGTCAGATTAAGTGC**
TGA

10 **SEQ ID NO:30**

Human T2R16 amino acid sequence

MIPIQLTVFFMIIYVLESLTIIIVQSSLIVAVLGREWLQVRRMLPVDMILISLGISRFCLQ
WASMLNNFCSYFNLNYVLCNLTITWEFFNILTFWLNSLLTVFYCIKVSSFTHHIFLWLRLW
15 RILRLFPWILLGSLMITCVTIIIPSAIGNYIQIQLLTMEHLPRNSTVTDKLENFHQYQFQA
HTVALVIPFILFLASTIFLMASLTKQIQHHSTGHCPNPSMKARFTALRSLAVLFIVFTSYF
LTILITIIGTLFDKRCWLWVWEAFVYAFILMHSTSLMLSSPTLKRILKGKC

20 **SEQ ID NO:31**

Human T2R16 nucleotide sequence

ATGATACCCATCCAACTCACTGTCTTCTTCATGATCATCTATGTGCTTGAGTCCTTGACA
ATTATTGTGCAGAGCAGCCTAATTGTTGCAGTGCTGGGCAGAGAATGGCTGCAAGTCAGA
25 AGGCTGATGCCTGTGGACATGATTCTCATCAGCCTGGGCATCTCTCGCTTCTGTCTACAG
TGGGCATCAATGCTGAACAATTTTGTCTCCTATTTTAATTTGAATTATGTACTTTGCAAC
TTACAATCACCTGGGAATTTTAAATATCCTTACATTCTGGTTAAACAGCTTGCTTACC
GTGTTCTACTGCATCAAGGTCTCTTCTTTCACCCATCACATCTTTCTCTGGCTGAGGTGG
AGAATTTTGAGGTTGTTTCCCTGGATATTACTGGGTTCTCTGATGATTACTTGTGTAACA
30 ATCATCCCTTCAGCTATTGGGAATTACATTCAAATTCAGTTACTCACCATGGAGCATCTA
CCAAGAAACAGCACTGTAACCTGACAACTTGAAAATTTTCATCAGTATCAGTTCCAGGCT
CATACAGTTGCATTGGTTATTCCTTTCATCCTGTTTCCCTGGCCTCCACCATCTTTCTCATG
GCATCACTGACCAAGCAGATACAACATCATAGCACTGGTCACTGCAATCCAAGCATGAAA
GCGCGCTTCACTGCCCTGAGGTCCCTTGCCGTCTTATTTATTGTGTTTACCTCTTACTTT

CTAACCATACTCATCACCATTATAGGTACTCTATTTGATAAGAGATGTTGGTTATGGGTC
TGGGAAGCTTTTGTCTATGCTTTCATCTTAATGCATTCCACTTCACTGATGCTGAGCAGC
CCTACGTTGAAAAG**GATTCTAAAGGGAAGTGCTAG**

5

SEQ ID NO:32

Human T2R17 amino acid sequence

MCSAXLLIILSILVVFAFVLGNVANGFIALINVNDWVKTQKISSTDQIVTALAFSRIGLL
10 XTLLIILLHWYATVFNSALYSLEVRIVPSNVSAIINHFSIWLATSLSIFYLFKIANFSNFI
FLHLKKRIKSVLLVILLGSLVFLICNLAVVTMDDSVWTKEFEGNVTWKIELRNAIHLSNM
TITNHASKLHTVHSDSNIFSAVSLFSXTMLANFTLFILTLISFLLLVCSPCKHLKMMQLH
GKGSQDLSTKVHIKPLQTVISFRMLFAIYFLCIITSTWNPRTQQSNLVFLLYQTLAIMYP
SFHSFILIMRSRKLKQTSLSVLCQVTCWVK

15

SEQ ID NO:33

Human T2R18 amino acid sequence

MFVGINIFFLVVATRGLVLGMLGNGLIGLVNCIEWAKSWKVSSADFILTSLAIVRIIRLY
20 LILFDSFIMVLSPHLYTIRKLVKLFITILWALINQLSI*FATCLSIFYLLKIANFSHSLFL
WLKWRMNGMIVMLLILSLFLLIFDSLVL EIFIDISLNIIDKSNLTLYLDESKTLYDKLSI
LKTLLSLTYVIPFLTLTSLLLLFISLVRHTKNLQNLGSRDSSTEAHKRAMKMVIAFL
LLFIINFISTLIGDWIFLEVENYQVMFMIMMILLA FPSGHSFIIILGNKLRQSSLRLW
25 HLKFSCLKAKPLTS

SEQ ID NO:34

Human T2R18 nucleotide sequence

30

ATGTTTCGTTGGAATTAATATTTTCTTTCTGGTGGTGGCAACAAGAGGACTTGTCTTAGGA
ATGCTGGGAAACGGGCTCATTGGACTGGTAAACTGCATTGAGTGGGCCAAGAGTTGGAAG
GTCTCATCAGCTGATTTTCATCCTCACCAGCTTGGCTATAGTCAGAATCATTCGACTGTAT
TTAATACTATTTGATTCATTTATAATGGTATTGTCCCCTCATCTATATACCATCCGTAAA

CTAGTAAACTGTTTACTATTCTTTGGGCATTAATTAATCAGTTAAGTATCTAGTTTGCC
 ACCTGCCTAAGCATTTTCTACTTGCTTAAGATAGCCAATTTCTCCCACTCCCTTTTCCTC
 TGGCTGAAGTGGAGAATGAACGGAATGATTGTTATGCTTCTTATATTGTCTTTGTTCTTA
 CTGATTTTTGACAGTTTAGTGCTAGAAATATTTATTGATATCTCACTCAATATAATAGAT
 5 AAAAGTAATCTGACTTTATATTTAGATGAAAGTAAACTCTCTATGATAAACTCTCTATT
 TTAAAACTCTTCTCAGCTTGACATACGTTATTCCCTTTCTTCTGACTCTGACCTCTTTG
 CTCCTTTTATTTATATCCTTAGTGAGACACACCAAGAATTTGCAGCTCAACTCTCTGGGC
 TCAAGGGACTCCAGCACAGAGGCCCATAAAAGGGCCATGAAAATGGTGATAGCCTTCCTC
 CTCCTTTTTATTATTAACCTTTATTTCCACTTTAATAGGAGATTGGATCTTCCTTGAGGTA
 10 GAGAATTATCAGGTCATGATGTTTATTATGATGATTTTACTTGCCTTTCCCTCAGGCCAC
 TCATTTATTATAATTTTGGGAAACAACAAGCTAAGACAGAGCTCCTTGAGACTACTGTGG
 CATCTTAAATTCTCTCTGAAAAAAGCAAAACCTTTAACTTCATAG

15 **SEQ ID NO:35**

Human T2R19 amino acid sequence

VTTLANLIPFTLSLICFLLLICSLCKHLKKMRLHSGKSQDPSTKVHIKALQTVTSFLMLF
 AIYFLCIITSTWNLRTQQSKLVLLLCQTVAIMYPSFHSFILIMGSRKLKQTFLSVLWQMT
 20 C

SEQ ID NO:36

Human T2R19 nucleotide sequence

25 CTGTAACACTCTAGCAAACCTCATACCCTTTACTCTGAGCCTAATATGTTTTCTGCTGT
 TAATCTGTTCTCTTTGTAAACATCTCAAGAAGATGCGGCTCCATAGCAAAGGATCTCAAG
 ATCCCAGCACCAAGGTCCATATAAAAGCTTTGCAAACCTGTGACCTCCTTCCTCATGTTAT
 TTGCCATTTACTTTCTGTGTATAATCACATCAACTTGAATCTTAGGACACAGCAGAGCA
 30 AACTTGTAACCTGCTTTGCCAACTGTTGCAATCATGTATCCTTCATTCCACTCATTCA
 TCCTGATTATGGGAAGTAGGAAGCTAAAACAGACCTTTCTTTCAGTTTTGTGGCAGATGA
 CATGCTGAGTGAAAGAAGAGAAACCCTCAACTCCATAGATTCACAAGGGGAGCATCGTGG
 GTCTTCTAGCAGAAAACAACTGATGGTGTCTGGAACATTTTATAT

[illegible]

Human T2R20 amino acid sequence

5 HLXRRKAKSVVLVIVLGSFLFLVCQLVMKNTYINVWTEECEGNVTWKIKLRNAMHLSNLT
V
AMLANLIPFTLTVISFLLLIYSLCKHLKKMQLHGKGSQDPSTKIHIALQTVTSFLVLLA
IYFLCLIIS

10 **SEQ ID NO:38**

Human T2R20 nucleotide sequence

15 T T C A T C A C T T A N A A A G G A A G G C T A A G A G T G T A G T T C T G G T G A T A G T G T T G G G G T C T T T G T
T C T T T T T G G T T T G T C A A C T T G T G A T G A A A A C A C G T A T A T A A A T G T G T G G A C A G A A G A A T
G T G A A G G A A A C G T A A C T T G G A A G A T C A A A C T G A G G A A T G C A A T G C A C C T T T C C A A C T T G A
C T G T A G C C A T G C T A G C A A A C T T G A T A C C A T T C A C T C T G A C C G T G A T A T C T T T T C T G C T G T
T A A T C T A C T C T C T G T G T A A A C A T C T G A A G A A G A T G C A G C T C C A T G G C A A A G G A T C T C A A G
A T C C C A G C A C C A A G A T C C A C A T A A A A G C T C T G C A A A C T G T G A C C T C C T T C C T C G T A T T A C
T T G C C A T T T A C T T T C T G T G T C T A A T C A T A T C C T T T T G

SEQ ID NO:39

Human T2R21 amino acid sequence

25 MPPGIGNTFLIVMMGEFII*MLGNGFIVLVNCIDW*GVK*SY*TTASSPAWLSPQSVNFG
*YYLIHL*QHYGHIYMPSIN*NLFIFFGH*PIT*LPGLLP*CFLLL*NTYFSHPCFIWL
RWRISRTLLELPLGSLLLLFFNLALTGGLSDLWINIYTIYERNSTWSLDVSKILYCSLWI
LVSLIYLLISFLLSLISLLLLILSLMRHIRNLQLNTMGPRDLRMKAHKRAMKMKMKMMVSF
LLFFLVHFSSLLPTGWIFLIQQK*QANFFVLLTSIIFPSSHSEVLILENCKLRQTAVGPL
30 WHLKCHLKRVKL

SEQ ID NO:40

Human T2R22 amino acid sequence

MATESDTNLLILAI AEFIISMLGNVFIGLVNCSEXIKNXKVFSADFILTCLAISHNGQLL
VILFDSFLVGLASHLYTTYRLXKNCIMLWT

5

SEQ ID NO:41

Human T2R22 nucleotide sequence

TATAGGGACNG**GTGATGCTTCGTACACTCTC**CAAGAAGAAACACTCCGTGAGGTATGTGAG
10 ACTGCATNCCTTAGTAGATCTNTTGGGATATATATTCATAATATAGAAAAANAGGCAAAG
ACTTNCTTAAGTATATGAGACTCTATCCAACAGCAGAAGGTTCTGATCAAGACTGGAAGT
GCAATANAAGCAATGAAGATAAGTATCAGATATGAATGCTCTTCTGCAATGGTCTGATTG
TNACATTATTAATGATACANAGTATTAAAACTTGGATTTTNTTGTCTCTGGAGATGGCC
ACCGAATCGGACACAAATCTTCTGATTCTGGCAATAGCAGAATTCATCATCAGCATGCTG
15 GGGAATGTGTTCAATTGGACTGGTAAACTGCTCTGAANGGATCAAGAACCANAAGGTCTTC
TCAGCTGACTTCATCCTCACCTGCTTGGCTATCTCTCACAATGGACAACTGTTGGTGATA
CTGTTTGATTCAATTTCTAGTGGGACTTGCTTCACATCTATATACCACATATAGACTANGA
AAAACTGTATTATGCTTTGGACATGACTAATCACTTGACACACTGCTTCGCACGTGCTA
GCATATTCTATTCTTAGATAGCCACTTCNCACTCCTT**GTCTCTGCTGAAGTGGGAT**

20

SEQ ID NO:42

Human T2R23 amino acid sequence

25 VAFVLGNVANGFIALVNVIDXVNTRKISSAEQILTALVVSRI GXTLXHSIP*DATRC*SA
LYRXEVRIVASN

SEQ ID NO:43

30 Human T2R23 nucleotide sequence

AGGGTTGAGTCGTGCTTATCTTCACTTAACCTAGTATANAANTACAGCATATAGCAAGGA
GAGAATGTATATGAAGAGGAGTGAATTTGAGTCTGTTTGAGAATAATGACCTTTTCTATT
TCTATAAAGACAGTTTTGAATTCATCTATTAGCATATGCTGGTGCTTGCCTGTTGACACT

AGTCACTGAATTTAAAGGCAGAAAATGTTATTGCACATTTAGTAATCAAGTGTTTCATCGA
AGTTAACATCTGGATGTTAAAGGACTCAGAACAAGTGTTACTAAGCCTGCATTTTTTTAT
CTGTTCAAACATGATGTGTTNTCTGCTCATCATTTTCATCAATTCTGGTAGAGTTGCATTT
GTTCTTGGAATGTNGCCAATGGCTTCATAGCTCTAGTAAATGTCATTGACTGNGTTAAC
5 ACACGAAAGATCTCCTCAGCTGAGCAAATTCTCACTGCTCTGGTGGTCTCCAGAATTGGT
NNTACTCTGNGTCATAGTATTCCTTGAGATGCAACTAGATGTTAATCTGCTCTATATAGG
NTAGAAGTAAGAATTGTTGCTTCTAATGCCTGAGCTCGTACGAACCATT

10 **SEQ ID NO:44**

Human T2R24 amino acid sequence

MATELDKIFLILAI AEFIISMLGNVFIGLVNCSEGIKNQKVFSADFILTCLAISTIGQLL
VILFDSFLVGLASHLYTTYRLGKTVIMLWHMTNHLTTWLATCLSIFYFFKIAHFPHSLFL
15 WLRWRMNGMIVMLLLLSLFLLI FDSLVL EIFIDISLNIIDKSNLTLYLDESKTLYDKLSI
LKTLLSLTSFIPFSLFLTSLFLFLSLVRHTRNLKLSSLGSRDSSTEAHRRAMKMVMSFL
FLFIVHFFSLQVANGIFFMLWNNKYIKFVMLALNAFPSCHSFILILGNSKLRQTAVRLLW
HLRNYTKTPNALPL

20

SEQ ID NO:45

Human T2R24 nucleotide sequence

ATGGCCACCGAATTGGACAAAATCTTTCTGATTCTGGCAATAGCAGAATTCATCATCAGC
25 ATGCTGGGGAATGTGTTTCATTGGACTGGTAAACTGCTCTGAAGGGATCAAGAACCAAAAG
GTCTTCTCAGCTGACTTCATCCTCACCTGCTTGGCTATCTCCACAATTGGACAACCTGTTG
GTGATACTGTTTGATTCAATTTCTAGTGGGACTTGCTTCACATTTATATACCACATATAGA
CTAGGAAAACTGTTATTATGCTTTGGCACATGACTAATCACTTGACAACCTGGCTTGCC
ACCTGCCTAAGCATTTTCTATTTCTTTAAGATAGCCCACTTCCCCCACTCCCTTTTCCTC
30 TGGCTGAGGTGGAGGATGAACGGAATGATTGTTATGCTTCTTATATTGTCTTTGTTCTTA
CTGATTTTTGACAGTTTAGTGCTAGAAATATTTATTGATATCTCACTCAATATAATAGAT
AAAAGTAATCTGACTTTATATTTAGATGAAAGTAAACTCTCTATGATAAACTCTCTATT
TTAAAACTCTTCTCAGCTTAACCAGTTTTATCCCCTTTTCTCTGTTCCCTGACCTCCTTG
CTTTTTTTATTTCTGTCCTTGGTGAGACATACTAGAAATTTGAAGCTCAGTTCCTTGGGC

TCTAGAGACTCCAGCACAGAGGCCCATAGGAGGGCCATGAAAATGGTGATGTCTTTCCTT
TTCCTCTTCATAGTTCATTTTTTTTCCTTACAAGTGGCCAATGGGATATTTTTTATGTTG
TGGAACAACAAGTACATAAAGTTTGTTCATGTTAGCCTTAAATGCCTTTCCTCGTGCCAC
TCATTTATTCTCATTCTGGGAAACAGCAAGCTGCGACAGACAGCTGTGAGGCTACTGTGG
5 CATCTTAGGA ACTATACAAAAACACCAAATGCTTTACCTTTGTAG

SEQ ID NO:46

Human T2R25 amino acid sequence

10

LSPFRMLFAIYFLCIITSTWNPRTQQSNLVFLLYQTLAIMYPSFHSFILIMRSRKLKQTS
LSVLCQVTCWVK

15

SEQ ID NO:47

Human T2R26 amino acid sequence

20

MPPGIGNTFLIVMMGEFII*MLGNGFIVLVNCIDVRSQMILLDNCILTSIAISTISQLWI
ILLDSFVTALWPHLYAFNKLIKFIHIFWALTNHLVTWLACCLSVFYFFKIAFYFSHPCFIW
LRWRISR TLLELPLGSLLLLFFNLALTGGLSDLWINIYTM YERNSTWSLDVSKILYCSLW
ILVSLIY LISFLLSLISLLLLILSLMRHIRNLQLNTMGPRDLRMKAHKRAMKMKMMMS
FLLFFLVHFSSLLPTGWIFLIQQK

25

SEQ ID NO:48

Human T2R27 amino acid sequence

30

LANLIDWAENQICLMDFILSSLAICRTLLLGCCVAIRCTYNDYPNIDAVNHNLIKIIITIF
DILRLVSK*LGIWFASYLSIFYLLKVALFHHAIFLWLKWRISR AVFTFLMIFLFFYISII
SMIKIKLFLDQC*YKI*EKLLEGRCE*SPPSC*PDAH*PGVVYSLYHFSYLMFLVCYLP
KGKHCTAVVIGDWLQRP RTEAYVRAMNIMIAFFFHLLYSLGTSLSVSYFLCKRKIVALG
AYLSYPLSHSFILIMENNKVRKAL

SEQ ID NO:49

Human T2R28 amino acid sequence

NICVLLIILSILVVSAFVLGNVANGFIALINVNDW

5

SEQ ID NO:50

Human T2R29 amino acid sequence

10 MQAALTAFFVLLFSLLSLLGIAANGFIVLVLGKEWL

SEQ ID NO:51

Human T2R30 amino acid sequence

15

MITFLPIIFSILVVVTFVLGNFSNGFIALVNSIEWVKTRKISSADQILTALVVS RVGLLW
VILLHWYANVFNSALYSSEVGAVASNISAIINHFSIWLATSLSIFYLLKIANFSNLI FLH
LKKRIRSVVLVILLGPLVFLICNLAVITMDDSVWTKEYEGNVTWKIKLRNAIHLSNMTVS
TLANLIPFILTLICFLLLICSLCKHLKMKQLHGKGSQDPSTKVHIKALQTVTSFLLLCAI
20 YFLSMIISVCNFRLEKQPVFMFCQAIIFSYPSTHPFILILGNKKLKQIFLSVLRHVRYW
VKDRSLRLHRFTRGALCVF

SEQ ID NO:52

25 Human T2R30 nucleotide sequence

ATGATAACTTTTCTACCCATCATTTTTTCCATTCTGGTAGTGGTTACATTTGTTCTTGGA
AATTTTTCCAATGGCTTCATAGCTCTAGTAAATTCATTGAGTGGGTCAAGACACGAAAG
ATCTCCTCAGCTGACCAAATCCTCACTGCTCTGGTGGTCTCCAGAGTTGGTTTACTCTGG
30 GTCATATTATTACATTGGTATGCAAATGTGTTTAATTCAGCTTTATATAGTTCAGAAGTA
GGAGCTGTTGCTTCTAATATCTCAGCAATAATCAACCATTTCAGCATCTGGCTTGCTACT
AGCCTCAGCATATTTTATTTGCTCAAGATTGCCAATTTCTCCAACCTTATTTTTCTCCAC
TTAAAGAAGAGAATTAGGAGTGTTGTTCTGGTGATACTGTTGGGTCCCTTGGTATTTTTG
ATTTGTAATCTTGCTGTGATAACCATGGATGACAGTGTGTGGACAAAAGAATATGAAGGA

AATGTGACTTGGAAGATCAAATTGAGGAATGCAATACACCTTCAAATATGACTGTAAGC
ACACTAGCAAACCTCATACCCTTCATTCTGACCCTAATATGTTTTCTGCTGTTAATCTGT
TCTCTGTGTAAACATCTCAAGAAGATGCAGCTCCATGGCAAAGGATCTCAAGATCCCAGC
ACCAAGGTCCACATAAAAGCTTTGCAAAGTGTGACCTCCTTTCTTCTGTTATGTGCCATT
5 TACTTTCTGTCCATGATCATATCAGTTTGTAAATTTTGGGAGGCTGGAAAAGCAACCTGTC
TTCATGTTCTGCCAAGCTATTATATTCAGCTATCCTTCAACCCACCCATTATCCTGATT
TTGGGAAACAAGAAGCTAAAGCAGATTTTCTTTCAGTTTTCGCGCATGTGAGGTACTGG
GTGAAAGACAGAAGCCTTCGTCTCCATAGATTACAAGAGGGGCATTGTGTGTCTTCTAG

10

SEQ ID NO:53

Human T2R31 amino acid sequence

MTTFIPIIFSSVVVVLVIGNFANGFIALVNSIERVKRQKISFADQILTALAVSRVGLLW
15 VLLLNWYSTVFENPAFYSEVVRTTAYNVWAVTGHFSNWLATSLSIFYLLKIANFSNLI FLH
LKRRVKSVILVMLLGPLLFLACQLFVINMKEIVRTKEFEGNMTWKIKLKSAMYFSXMTVT
IGAXLVPFTLSLISFLMLICSLCKHLKKMQLHGEQSQDLSTKVHIKALQTLISFLLLCAI
FFLFLIVSVWSPRRLRNDPVVMVSKAVGNIYLAFDSFILIWRTKKLKHTFLLILCQIRC

20

SEQ ID NO:54

Human T2R31 nucleotide sequence

ATGACAACTTTTATACCCATCATTTTTTCCAGTGTGGTAGTGGTTCTATTTGTTATTGGA
25 AATTTTGCTAATGGCTTCATAGCATTGGTAAATTCCATTGAGCGGGTCAAGAGACAAAAG
ATCTCTTTTGCTGACCAGATTCTCACTGCTCTGGCGGTCTCCAGAGTTGGTTTGCTCTGG
GTATTATTATTAAATTGGTATTCAACTGTGTTTAATCCAGCTTTTTTATAGTGTAGAAGTA
AGAACTACTGCTTATAATGTCTGGGCAGTAACCGGCCATTTCAAGCAACTGGCTTGCTACT
AGCCTCAGCATATTTTATTTGCTCAAGATTGCCAATTTCTCCAACCTTATTTTTCTTCAC
30 TTAAAGAGGAGAGTTAAGAGTGTCATTCTGGTGATGCTGTTGGGGCCTTTACTATTTTTG
GCTTGTCAACTTTTTGTGATAAACATGAAAGAGATTGTACGGACAAAAGAATTTGAAGGA
AACATGACTTGGAAGATCAAATTGAAGAGTGCAATGTACTTTTCANATATGACTGTAACC
ATTGGAGCANACTTAGTACCCTTTACTCTGTCCCTGATATCTTTTCTGATGCTAATCTGT
TCTCTGTGTAAACATCTCAAGAAGATGCAGCTCCATGGAGAAGGATCGCAAGATCTCAGC

ACCAAGGTCCACATAAAAGCTTTGCAAACCTCTGATCTCCTTCCTCTTGTTATGTGCCATT
TTCTTTCTATTCCCTAATCGTTTCGGTTTGGAGTCCTAGGAGGCTGCGGAATGACCCGGTT
GTCATGGTTAGCAAGGCTGTTGGAAACATATATCTTGCAATTCGACTCATTCATCCTAATT
TGGAGAACCAAGAAGCTAAAACACACCTTTCTTTTGATTTTGTGTCAGATTAGGTGCTGA

5

SEQ ID NO:55

Human T2R32 amino acid sequence

10 HSFMLTMGSRKPKQTFLSAL

SEQ ID NO:56

Human T2R33 amino acid sequence

15

MVYFLPIIFSILVVFAFVLGNFSNGFIALVNVIDWVKRQKISSADQILTALVVS RVGLLW
VILLHWYANVFNSALYSLEVRIVASNISAVINHFSIWLAASLSIFYLLKIANF SNLI FLH
LKKRIKSVVLVILLGPLVF LICNLAVITMDERVWTK EYEGNVTWKIKLRNAIHLSSLT VT
TLANLIPFTLSLICFLL LICSLCKHLKKMQLH SKGSQDPSTKVHIKALQTVISFLMLCAI
20 YFLSIMISVWNLRSL ENKPVFMFCKAIRFSYPSIHPFILIWGNKKLKQTF LSVFWQVRYW
VKGEKPSSP

SEQ ID NO:57

25 Human T2R33 nucleotide sequence

ATGGTATATTTTCTGCCCATCATTTTTTCCATTCTGGTAGTGT TTGCATTTGTTCTTGGA
AATTTTTCCAATGGCTTCATAGCTCTAGTAAATGTCATTGACTGGGT TAAGAGACAAAAG
ATCTCCTCAGCTGACCAAATTCTCACTGCTCTGGTGGTCTCCAGAGTTGGTTTACTCTGG
30 GTCATATTATTACATTGGTATGCAAATGTGTTTAATTCAGCTTTATATAGTTTAGAAGTA
AGAATTGTTGCTTCTAATATCTCAGCAGTAATCAACCATTT CAGCATCTGGCTTGCTGCT
AGCCTCAGCATATTTTATTTGCTCAAGATTGCCAATTTCTCCAACCTTATTTTTCTCCAC
CTAAAGAAGAGAATTAAGAGTGTTGTTCTGGTGATACTGTTGGGGCCCTTGGTATTTCTG
ATTTGTAATCTTGCTGTGATAACCATGGATGAGAGAGTGTGGACAAAAGAATATGAAGGA

AATGTGACTTGGAAGATCAAATTGAGGAATGCAATACACCTTTCAAGCTTGACTGTAAC
 ACTCTAGCAAACCTCATACCCTTTACTCTGAGCCTAATATGTTTTCTGCTGTTAATCTGT
 TCTCTTTGTAAACATCTCAAGAAGATGCAGCTCCATAGCAAAGGATCTCAAGATCCCAGC
 ACCAAGGTCCACATAAAAGCTTTGCAAACGTGATCTCCTTCCTCATGTTATGTGCCATT
 5 TACTTTCTGTCCATAATGATATCAGTTTGAATCTTAGGAGTCTGGAAAACAAACCTGTC
 TTCATGTTCTGCAAAGCTATTAGATTCAGCTATCCTTCAATCCACCCATTCATCCTGATT
 TGGGGAAACAAGAAGCTAAAGCAGACTTTTCTTTCAGTTTTTTGGCAAGTGAGGTACTGG
 GTGAAAGGAGAGAAGCCTTCATCTCCATAG

10

SEQ ID NO:58

Human T2R34 amino acid sequence

GSSRXKPPRI PHKKLCKLGPSFPHNNLPIYFLCXNHIVLEFLKMRPKKKCSLMLCQAFGI
 15 IYPSFHSFILXWGNKTLKQTFLSVXWQVTCWAKGQNQSTP

SEQ ID NO:59

Human T2R35 amino acid sequence

20

NAIRPSKLWTVTEADKTSQPGTSANKIFSAGNLISHVNMSRRMQLHGKGSQHLSTRVHIK
 AXQTVISFLMLXAIYFLCLITSTWNPRTQQSKLVFLLYQTLGFMYLLFHSFILTMGSRKP
 KQTFLSAL

25

SEQ ID NO:60

Human T2R36 amino acid sequence

MICFLLIILSILVVFAFVLGNFSGFIALVNVIDWVKRQKISSADQILTALVVSrvGLLW
 30 VILLHWYSNVLNSALYSSEVIIIFISNAWAIINHFSIWLATSLSIFYLLKIVNFSRLIFHH
 LKRKAKSVVLVIVLGPLVFLVCHLVMKHTYINVWTKEYEGNVTWKIKLRNAIHLNLTVS
 TLANLIPFTLTLSIFLLLIYSLCKHLKKMQLHGKGSQDPSTKVHIKALQTVTSFLLLCAI
 YFLSMIISVCNFRLEKQPVFMFCQAIIFSYPSTHPPFILILGNKKLKQIFLSVFWQMRYW
 VKGEKPSSP

SEQ ID NO:61

Human T2R36 nucleotide sequence

5
ATGATATGTTTTCTGCTCATCATTTTATCAATTCTGGTAGTGTTCATTGTTCTTGGA
AATTTTTCCAATGGCTTCATAGCTCTAGTAAATGTCATTGACTGGGTCAAGAGACAAAAG
ATCTCCTCAGCTGACCAAATCCTCACTGCTCTGGTGGTCTCCAGAGTTGGTTTACTCTGG
GTAATATTATTACATTGGTATTCAAATGTGTTGAATTCAGCTTTATATAGTTCAGAAGTA
10 ATAATTTTTATTTCTAATGCCTGGGCAATAATCAACCATTTAGCATCTGGCTTGCTACT
AGCCTCAGCATATTTTATTTGCTCAAGATCGTCAATTTCTCCAGACTTATTTTTTCATCAC
TTAAAAAGGAAGGCTAAGAGTGTAGTTCTGGTGATAGTGTTGGGTCCCTTGGTATTTTTG
GTTTGTACCTTGTGATGAAACACACGTATATAAATGTGTGGACAAAAGAATATGAAGGA
AATGTGACTTGGAAGATCAAACCTGAGGAATGCAATACACCTTTCAAACCTGACTGTAAGC
15 AACTAGCAAACCTTGATACCCTTCACTCTGACCCTGATATCTTTTCTGCTGTTAATCTAC
TCTCTGTGTAAACATCTCAAGAAGATGCAGCTCCATGGCAAAGGATCTCAAGATCCCAGC
ACCAAGGTCCACATAAAAGCTTTGCAAACCTGTGACCTCCTTTCTTCTGTTATGTGCCATT
TACTTTCTGTCCATGATCATATCAGTTTGTAATTTTGGGAGGCTGGAAAAGCAACCTGTC
TTCATGTTCTGCCAAGCTATTATATTCAGCTATCCTTCAACCCACCCATTCATCCTGATT
20 TTGGGAAACAAGAAGCTAAAGCAGATTTTCTTTCAGTTTTTTGGCAAATGAGGTACTGG
GTGAAAGGAGAGAAGCCTTCATCTCCATAG

SEQ ID NO:62

25 Human T2R37 amino acid sequence

MITFLPIIFSILIVVTFVIGNFANGFIALVNSIEWVKRQKISSADQISHCSGGVQNWFTL
GHIITLVCNCV*FGFI*IRSKNFWF*CLSNQAFQHVGVTSLSIFHLLKTANFSNLIFLH
LKKRIKSVGLVILLGPLLFFICNLFVINMDES VWTKEYEGNVTWKIKLRSAMYHSNMTLT
30 MLANFVPFTLT LISFLLLICSLCKHLKKMQLHGKGSQDPSTKVHIKALQTVTSFLLLCAI
YFLSMIISVCNLGRLEKQPVFMFCEAIIFSYPSTHPFILILGNKKLKQIFLSVLRHVRYW
VKGEKPSSS

SEQ ID NO:63

Human T2R37 nucleotide sequence

ATGATAACTTTTCTGCCCATCATTTTTTCCATTCTAATAGTGGTTACATTTGTGATTGGA
5 AATTTTGCTAATGGCTTCATAGCTCTAGTAAATTCCATTGAGTGGGTAAAGAGACAAAAG
ATCTCATCAGCTGACCAAATTTCTCACTGCTCTGGTGGTGTCCAGAATTGGTTTACTCTG
GGTCATATTATTACATTGGTATGCAACTGTGTTTAATTTGGCTTCATATAGATTAGAAGT
AAGAATTTTTGGTTCTAATGTCTCAGCAATAACCAAGCATTTTCAGCATGTGGGTGTTACT
AGCCTCAGCATATTTTCAATTTGCTCAAGACTGCCAATTTCTCCAACCTTATTTTTCTCCAC
10 CTAAAGAAGAGGATTAAGAGTGTTGGTTTGGTGATACTATTGGGGCCTTTGCTATTTTTTC
ATTTGTAATCTTTTTTGTGATAAACATGGATGAGAGTGTATGGACAAAAGAATATGAAGGA
AACGTGACTTGGAAGATCAAATTGAGGAGTGCAATGTACCATTCAAATATGACTCTAACC
ATGCTAGCAAACCTTTGTACCCTTCACTCTGACCCTGATATCTTTTCTGCTGTTAATCTGT
TCTCTGTGTAAACATCTCAAGAAGATGCAGCTCCATGGCAAAGGATCTCAAGATCCCAGC
15 ACCAAGGTCCACATAAAAGCTTTGCAAACGTGACCTCCTTTCTTCTGTTATGTGCCATT
TACTTTCTGTCCATGATCATATCAGTTTGTAATTTGGGGAGGCTGGAAAAGCAACCTGTC
TTCATGTTCTGCGAAGCTATTATATTCAGCTATCCTTCAACCCACCCATTCATCCTGATT
TTGGGAAACAAGAAGCTAAAGCAGATTTTTCTTTCAGTTTTGCGGCATGTGAGGTACTGG
GTGAAAGGAGAGAAGCCTTCATCTTCATAG

20

SEQ ID NO:64

Human T2R38 amino acid sequence

25 MLTLTRIRTVSYEVRSTFLFISVLEFAVGFLTNAFVFLVNFWDVVKRQPLSNSDCVLLCL
SISRLFLHGLLFLSAIQLTHFQKLSEPLNHSYQAIIMLWMIANQANLWLAACLSLLYCSK
LIRFSHTFLICLASWSPGRSPVPS

30 **SEQ ID NO:65**

Human T2R39 amino acid sequence

LRNAGLNDSTNAKLVRNNDLLLINLILLPLSVFVMCTSMLEFVSLEYKMHWMQSESHKLSS
ARTEAHINALKTVTTFFCFFVSYFAAFMANMTFRIPYRSHQFFVVKEIMAAYPAGHSVII
VLSNSKFKDLFRMICLQKE

5

SEQ ID NO:66

Human T2R40 amino acid sequence

10 SQYSLGHSYVVIFGYGQMKKTFILGILWHLKCGLKGRALLATQVGLREKSTRSLGVI FLAS
SYSFFVYVLCH

SEQ ID NO:67

Human T2R41 amino acid sequence

15

MITFLLIILSILVVFAFVLGNFSGFIALVNVIDWVNTRKISSADQILTALAVSRVGLLW
VILLHWYANVLNPALYSSEVIIIFISNISAIINHFSIWLATSLSIFYLLKIVNFSRLIFHH
LKRKAKSVVLVIVLGPLVFLVCHLVMKHTYINVWTKEYEGNVTWKIKLRNAIHLSNLTVS
TLANLIPFTLTLSIFLLLICSLCKHLKKMQLHSGKSQDPSTKVHIKALQTVTSFLMLFAI
20 YFLYLITSTWNL*TQQSKLVFMFCQTLGIMYPSFHSFILIMGSRKLKQTFLSVLCQVTCL
VKGQQPSTP

SEQ ID NO:68

25 Human T2R42 amino acid sequence

FIGLTDICIAWMRNQKLCMVGFILTRMALARINIL

30

SEQ ID NO:69

Human T2R43 amino acid sequence

LELIFS*KVVATRGLVLGMLGNGLIGLVNCIEWAKSWKVSSADFILTSLAIVRIIRLYLI
LFDSFIMVLSPHLYTXXXXXXXXXXXXXXXXXXXXXXXXXSLSI FHWFKTANFSNLIFLPLK

EED*NVWLGDVAGALGIFHL*SCSENHG*EVCGQKNMKEFCSGMIKLRNAIQLSNLTVTM
PANVTPCTLTLISFLLLIYSPCKHVKKMQLHGKGSQHLSTKVHIKVLQTVISFFLLCAIY
FVSVIISVWSFKNLENKPVFMFCQAIGFSCSSAHPFILTGMGNKKLKQTYLSVLWQMR

5

SEQ ID NO:70

Human T2R44 amino acid sequence

MITFLPIIFSILIVVIFVIGNFANGFIALVNSIEWVKRQKISFVDQILTALAVSRVGLLW
10 VLLHWHYATQLNPAFYSEVRITAYNVWAVTNHFSSWLATSLSMFYLLRIANFSNLIFLR
IKRRVKSIVLVILLGPLLFLVCHLFVINMDETVWTKEYEGNVTWKIKLRSAMYHSNMTLT
MLANFVPLTLTLISFLLLICSLCKHLKKMQLHGKGSQDPSTKVHIKALQTVTSFLLLCAL
YFLSMIISVCNLGRLEKQPVFMFCQAIIFSYPSTHPPFILILGNKKLKQIFLSVLRHVRYW
VKDRSLRLHRFTRGALCVF

15

SEQ ID NO:71

Human T2R45 amino acid sequence

MATELDKIFLILAI AEFIISMLGNVFIGLVNCSEGIKNQKVFSADFILTCLAISTIGQLL
20 VILFDSFLVGLASHLYTTYRLGKTVIMLWHMTNHLTTWLATCLSIFYFFKIAHFPHSLFL
WLRWRMNGMIVMLLILSLFLLIFDSLVL EIFIDISLNIIDKSNLTLYLDESKTLYDKLSI
LKTLLSLTSFIPFSLFLTSLLFLEFLSLVRHTRNLKLSSLGSRDSSTEAHRRAMKMVMSFL
FLFIVHFFSLQVANWIFFMLWNNKCIKFVMLALNAFPSCHSFILILGNSKLQQTAVRLLW
25 HLRNYTKTPNPLPL

SEQ ID NO:72

Human T2R46 amino acid sequence

30

MSFLHIVFSILVVVAFILGNFANGFIALINFIWVKKQKISSADQIIADKQSPELVCSG

SEQ ID NO:73

Human T2R47 amino acid sequence

MLNALYSILIIIIINI*FLIGILGNGFITLVNGIDWVKM*KRSSILTALTISRICLISVIM
VRWFI

5

SEQ ID NO:74

Human T2R48 amino acid sequence

10 VSRVGLLWVILLHWYSTVLNPTSSNLKVIIIFISNAWAVTNHFSIWLATSLSIFYLLKIVN

SEQ ID NO:75

Human T2R49 amino acid sequence

15

TVTMLANLVPFTVTTLISFLLLVCSLCKHLKMKMHLHGKGSQDPSTKVHIKVLQTVISFLLL
CAIYFVSVIISS

20 **SEQ ID NO:76**

Human T2R50 amino acid sequence

MITFLPIIFSILVVVTFVIGNFANGFIALVNSTEWVKRQKISFADQIVTALAVSRVGLLW
VLLLNWYSTVLNPAFYVELRTTAYNIWAVTGHFSNWPATSLSIFYLLKIANFSNLI FLR
25 LKRRVKSVILVLLGPLLFLACHLFVVNMNQIVWTKEYEGNMTWKIKLRRAMYLSDTT VT
MLANLVPFTVTTLISFLLLVCSLCKHLKMKQLHGKGSQDPSTKVHIKVLQTVISFFLLCAI
YFVSVIISVWSFKNLENKPVFMFCQAIGFSCSSAHPFILIWGNKKLKQTYLSVLWQMRY

30 **SEQ ID NO:77**

Rat T2R01 amino acid sequence

MMEGHILFFFLVVMVQFVTGVLANGLIVVVHAIDLIMWKKMAPLDLLLFCLATSRIILQL
CILFAQLCLFSLVRHTLFEDNITFVFIINELSLWFATWLGVFYCAKIATIPHPLFLWLKM

RISRLVPWLILGSVLYVIIITTFIHSRETSAILKPIFISLFPKNATQVGTGHATLLSVLVL
GLTLPLFIFTVAVLLLIYSLWNYSRQMRMTVGTREYSGHAHISAMLSILSFLILYL SHYM
VAVLISTQVLYLGSRTFVFCLLVIGMYPsiHSIVLILGNPKLKRNAKMFIVHCKCCHCTR
AWVTSRSPRLSDLVPVPPTHPSANKTSCSEACIMPS

5

SEQ ID NO:78

Rat T2R01 nucleotide sequence

10 CAGGAATCATAAATGGCTGAAACTGGGCAGAACTCTATGCATTATTTAAAGAAGTCATTG
GTTTGTCAATTCTTAAATGATGGAAGGGCATATACTCTTCTTCTTTTGGTTGTGATGGT
GCAGTTTGTCACTGGGGTCTTGGCAAATGGCCTCATTGTGGTTGTCCATGCTATTGACTT
GATCATGTGGAAGAAAATGGCCCCGTTGGATCTGCTTCTATTTTGCCTGGCGACTTCTCG
GATCATTCTGCAGTTATGTATATTGTTTGCACAATTGTGTCTATTCTCTTGGTGAGACA
15 CACTTTATTTGAGGACAATATTACCTTTGTCTTCATCATAAATGAACTGAGTCTTTGGTT
TGCTACATGGCTCGGTGTTTTCTACTGTGCCAAGATTGCTACCATTCCCTACCCACTCTT
TCTGTGGCTGAAGATGAGGATATCCAGGTTGGTACCATGGCTGATCCTGGGATCTGTGCT
CTATGTAATTATTACTACTTTTCATCCATAGCAGAGAGACTTCAGCAATCCTTAAACCAAT
TTTTATAAGCCTTTTTCTTAAATGCAACTCAAGTCGGAACAGGGCATGCCACACTACT
20 CTCAGTCCTGGTCCTTGGGCTCACACTGCCGTTGTTTCATCTTTACTGTTGCTGTTCTGCT
CTTGATATACTCCCTGTGGAATTATAGCAGGCAGATGAGGACTATGGTAGGCACCAGGGA
GTATAGCGGACATGCTCACATCAGTGCAATGCTGTCCATTCTATCATTCCCTCATCCTCTA
TCTCTCCCACTACATGGTGGCTGTTCTGATCTCTACTCAAGTCCTCTACCTTGAAGCAG
AACCTTTGTATTCTGCTTACTGGTTATTGGTATGTACCCCTCAATACACTCGATTGTCTT
25 AATTTTAGGAAATCCTAAGCTGAAACGAAATGCAAAAATGTTTCATTGTCCATTGTAAGTG
TTGTCATTGTACAAGAGCTTGGGTCACTCAAGGAGCCCAAGACTCAGTGACTTGCCAGT
GCCTCCTACTCATCCCTCAGCCAACAAGACATCCTGCTCAGAAGCCTGTATAATGCCATC
CTAATTGTCCAGCCTGAGGTTTAATCCTAGGTTTGGTACTATTTCAAAGAGTAAAGTTGA
TCATTAAAGCACAAACATATGTTGGTGGATGACATCAAGGTCCATATCCCAGTTGTCAATT
30 GTAAACCTCACCTTGCAAGATGATGTCACTGAGAAAGCAGGACAAATGGAGTCTAGGTCC
TTCTGTATGACTTGCTGCAGTATATGTGAATCTATAATTTTCTCCAAAAAACAAAAAA
AAAAAAAAAA

SEQ ID NO:79

Rat T2R02 amino acid sequence

5 MFSQKTNYSHLFTFSIIIFYVEIVTGILGNGFIALVNIMDWLKRRRISTADQILTALALTR
LIYVWSVLICILLFLCPHLSMRPEMFTAIGVIWVVDNHFSIWLATCLGVFYFLKIASFS
NSLFLYLKWRVKVVLMIILISLIFLMLNISSLGMYDHFSIDVYEGNMSYNLVDSTHFPR
IFLFTNSSKVFLIANSSHVFLPINSLFMLIPFTVSLVAFFVLFLSLWKHHKKMQVNAKGP
RDASTMAHTKALQIGFSFLLLYAIYLLFIITGILNLDLMRCIVILLFDHISGAVFSISHS
FVLILGNSKLRQATLSVLPCLRCRSKDMDTVVF

10

SEQ ID NO:80

Rat T2R02 nucleotide sequence

15 ATTTTGCTCCACTATTTTGCTCTTCTGCAGTAACACAGACCACAAAACAATGGAGCCAAT
GGGTCAAGAGCTGAAACTTCAGGAAGTGGGAGCCAAATTTTCTTTGTGATAGGTGGCAT
ATGAGAATTCATTATTTGATGCAGCTTCTGAAAAGTGGATGTGAAATACTGGATGAAGCA
GAGGTGATGACCCCTTTGAAATTAAAAAGCCAAGATGTTTCATGGAGAAATTATAAAACAA
TATCTGGGAAATTTGATGCTTCCTAATCGGGTGTAATGGGATTTTAAATGATGAACATT
20 TTGAATTTCCAATGACCATTATGTAAAGTTTTTAAACACAGTAGAGACATCATAAATTGA
AGCATGTTCTCACAGAAAACAACTACAGCCATTTGTTTACTTTTTCAATTATTTTTTAT
GTGGAAATAGTAACAGGAATCTTAGGAAATGGATTCATAGCACTAGTGAATATCATGGAC
TGGCTCAAGAGGAGGAGGATCTCTACTGCAGATCAGATTCTCACTGCTTTGGCCCTTACC
AGACTCATTTATGTGTGGTCTGTACTCATTTGTATATTGTTACTATTTCTGTGCCACAT
25 TTGTCTATGAGACCAGAAATGTTTACAGCGATAGGTGTTATCTGGGTAGTGGATAACCAC
TTCAGCATCTGGCTTGCTACATGTCTTGGTGTCTTTTATTTCTCCTCAAAATAGCCAGTTTT
TCTAACTCTTTGTTTCTTTACCTAAAGTGGAGAGTTAAAAAGTGGTTTTAATGATAATA
CTGATATCACTGATTTTCTTGATGTTAAACATTTTCATCATTAGGGATGTATGATCATTTT
TCAATTGATGTTTATGAAGGTAATATGTCTTATAATTTGGTGGATTCAACACATTTTCCC
30 AGAATTTTCTTATTCACAACTCATCTAAGGTCTTCTTAATCGCCAATTCATCCCATGTT
TTCTTACCCATCAACTCACTCTTCATGCTCATACCCTTCACAGTTTCCCTGGTAGCTTTT
TTCGTGCTCTTTCTCTCACTGTGGAAGCATCACAAGAAGATGCAGGTCAATGCCAAAGGA
CCCAGAGATGCCAGCACCATGGCCACACAAAAGCCTTGCAAATTGGGTTCTCCTTCCTC
CTGCTGTATGCAATATACTTACTTTTCATTATCACAGGAATTTTGAACCTTGACTTGATG

AGATGTATAGTAATACTTTTATTTGACCACATATCTGGAGCAGTTTTTTCTATAAGCCAC
 TCATTTGTGCTGATTCTGGGAAACAGTAAGCTGAGACAAGCCACTCTTTCTGTGCTGCCT
 TGTCTTAGGTGCCGGTCCAAAGATATGGACACTGTCGTTTTCTAAATAAATTCCAGAGTAC
 ATTATGCAAAATCTTGAGGGTGATCAGTTCATAGAAAAAGTAATCTTAGAGGGGAAAATA
 5 AAATATTGGGGCTTCAAATGTTGGATGGGTAATACATAGGAAGGCAGGACAAGGATGAAG
 GAGACTAGCATTATATAAGTGATTTACAGGGGAAATGGGAAAGAGGGCTTTTATATAAT
 GAAGAAGAAGATAAATGATGAAGGATGAGGAAGAGTTAAATATGTAAATGACAATAGAG
 ATGGCATCATGCCGTTTTAAGAAATTTGGAATGCATATGTATGTTTATATATTTTTTAAAT
 TTTTATTGAATATATTTATTTACATTTTAAATGTTATCCTGTTTCCCCCACCCAACCTCC
 10 CACCTCTTCCCACCTCCTTGCCCTGACATTCCCCTGCACTGGGGAATCCAGCCTTGACAG
 GACCAAGGGCTTCTCCTCCCTTTGTTGCCAACAAGGCCATTCTTTGCTACATGTGCAGCA
 GGAGCCATGGATCTGTCTATGTGTACTCTTTGGATGGTGGTTTAGTCCCTGGGAGCTCTT
 GTTGGTTGGTATTGTTGTTCTTATGGTGTTGCAACTCCCTTCAGCTCCTTCAATCCTTCC
 TGTAACTCCTCCAATGTGGACCCTGTTCTCAGTCCAATGGTTGACTATGAGCATTACCT
 15 CTGTGATTGTCATGCTCTGGCACAGCTTCTCAGAAGACAGCTACATCAGTCTCCTATAAG
 AGTGCACCTCATGGCATCAGCAATGTTGTCTTGATTTGGTGTCTGTATGTATATGGGCTG
 GATCCCAGGTGGGGCAGGCGCTGAATGGTCATTCCTTCAGTCTTTGCTCCAACTTTGTC
 TTTATATCTCCTATGAATATTTTTGTTCCCCCTTATAAGAATGACTGAAGTATCCACACT
 TTGGCCATCCTTCTTCATGAGCTTCATGTGGTCTGTGAATTGTACATTGTGTAATCCAAG
 20 CTTTTGGGCTAATATCCAATTATAGTGAGTGCATACCAAAAAAAAAAAAAAAAAAAAAA
 AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

SEQ ID NO:81

25 Rat T2R03 amino acid sequence

MVPTQVTIFSIIMYVLESLVIIVQSCTTVAVLFWREWMHFQRLSPVEIILISLGISHFCLQ
 WTSMLYNFGTYSRPVLLFWKVSVVWEFMNVLTFWLTSLLAVLYCVKVSSFHPVFLWLRL
 KILKLVLWLLLGALIASCLSIIPSVVKYHIQMELLTLDHLPKNSSLILRLQMFWEYFSNP
 30 FKMIGFGVPFLVFLISIIILLTVSLVQHWGQMKHYSSSSSSSLRAQCTVLKSLATFFIFFTS
 YFLTIVVSFIGTVFDKKSFWVCEAVIYGLVCIHFTSLMMSNPTLKKALRLQFWSPSS

SEQ ID NO:82

Rat T2R03 nucleotide sequence

GCATGGTGCCAACCCAAGTCACCATCTTCTCTATCATCATGTATGTGCTTGAGTCCTTAG
TCATAATTGTGCAAAGTTGCACAACGGTTGCAGTGCTGTTTCAGAGAGTGGATGCACTTTC
5 AAAGACTGTCGCCGGTGGAAATAATTCTCATCAGCCTGGGCATTTACATTTCTGTCTAC
AGTGGACATCGATGCTGTACAACTTTGGTACCTACTCTAGGCCTGTCCTTTTATTTTGA
AGGTATCGGTCTGCTGGGAGTTCATGAACGTTTTGACATTCTGGCTAACCAGTTTGCTTG
CTGTCCTCTACTGTGTCAAGGTCTCTTCCTTCTCTCACCCCGTCTTCCTCTGGCTGAGGT
TGAAAATTTTGAAACTGGTTCTCTGGTTGCTATTGGGCGCTCTGATAGCTTCTTGTTTGT
10 CAATCATCCCTTCTGTTGTTAAATATCATATCCAGATGGAATTACTACCCTAGATCATT
TACCCAAAAACAGTTCTTTGATTCTAAGACTGCAAATGTTTCGAGTGGTATTTTTCTAATC
CTTTCAAATGATTGGGTTTGGCGTTCCCTTTCCTCGTGTTCCCTGATTTCTATCATCTTAC
TCACAGTCTCGCTGGTCCAGCATTGGGGGCAGATGAAACACTACAGCAGCAGCAGCTCCA
GCCTGAGAGCTCAGTGCACTGTTCTGAAGTCTCTTGCCACCTTCTTCATCTTCTTCACAT
15 CCTATTTTCTGACTATAGTCGTCTCCTTTATTGGCACCGTGTTTGATAAGAAGTCATGGT
TCTGGGTCTGCGAAGCTGTCATCTATGGTTTAGTCTGTATTCACTTCACTTCCCTGATGA
TGAGCAACCCTACACTGAAAAAAGCACTCAGGTTGCAGTTCTGGAGCCCAGAGTCTTCCT
AAGGCAGGGAATTCAGTGAAGCCTCTGGGGTAAGGAGGCTTTGCATTGGCACAGTTCTTA
GAGTGAAATGCAAACGTGGACACGAACTTCATTCTCTTTCATGTCCACAGATGGATGGAT
20 CTATAAATCATCACCAATCTTCCCTGTATTCTGACCCATCCTTTTCTGTCTATCCATA
GTCCCCAGGTTGGTTTTGATTTTTCTCATGATCACACCTTAGCTTTAGCCACCGTTGCAA
TATCAAACATGATCTATATGTTACAGCCAAAATCATTCTCACAATTGTCAATTGCTTCAC
AAATTCAGATAAATCCCCCTTCTGTGAGGAATGTATTGTCTGTGCATTCAATGCTCACC
ATGCTAAGCCATTCAATCCCTTCCCTAACTTGAGTTTAAGAAGAAAATGTCTTACTGTTGC
25 CCATGTCCTATTGTGCTGCTTCTGGATGTTTTATGCAGTGATTTAGACACACGCCCTTGC
CTGTCTCCAAATACTGGCCCTTTATTCCTTTATAAGTCTAGTAGAAAATGAACTCGTCTT
TACTTCATTGACGAAGACATTGTATTCTTCCCCAAAATAGTGTTTAACTACTCTAGTCTC
ATCCATAATATCCCTAAATATCAGTGATTTTCAGTGAGTAAACCTGACAACAGTTATTGC
TTTGACTCTTAATTCAATTGTGCTGTAAATAGAGGAAACATTCTAGAACATTTCCATAT
30 TAATTTGTGCTTGTAGCAAACCAAAATTCTCCCAGTTGGGTAAAATATCAAAGCACA
GAGTAATCAATTTTGAAATCACTCAGAAGACATCATTGTTCTATATATGTTTTTTTTAAA
CTTCCCTCTAACAAGTATCAGATCTTTGCCTTTACAGGGTCTGGTCTTACCATGACTATA
TTTTATCACCATGACCTATTTTCTCTTCATCTCTTTGTTTTCACTAACTCAGTAGCAACC
AAATATCACATTAATAGCTAACTCTGGGCACTTATTTCTCAGCCTTTATCTATTCCAGAC

ACTTTCAATGTATTTCTGCTAAACACAATGACATCTCTTTTTGTGTTCTAACGACAAGGA
 ATCATAACTTTCCAACCTTTTATACATGGTAGACATATTTGGTGAACCTTAACCTCTGACTC
 TTTCTTTAGAAGACTGAAACTACTCCGGAAAGCAAGCCTTCTGATGGAGAAATAGATACG
 GGTATCGTGATTCAATTGTGAAAGTGAATTCCGGTGCCTGGAAAGAAATGGATATTTTTTT
 5 TTCTCTTGAGTGTGTCACTCTGACATATGTTCCATGTTGAATCCATATTTGATACTGATA
 GCATGAATGTAAGTAAAGCATGTATGTAAGTAAAGACTGCTACCAAACCTTCGATTCAAC
 TTTCTCAGCAGTATCCCTGATATTGCATAAGAAAGAAAAACACGCTGTCCTACTTGAA
 GAAGGACGTGTTCCATGCAATGTGGATGTGTCCCAGGCTACATTGGCTCAACTGCAGCTG
 AAGGTGGGATGGGAAATGGTATAGTTAGTAATGTCTGCTGAGCTGTCTCACTGGAAAGGA
 10 TTCTGAGCAGAGTAAATGTAAGCAATGTGGCCAAGGTCTCCTAGGAATGGGTTGTAAGCT
 TGTAAGGAGTTGGGTTGTAAGAGTTTGGGATCCTTTCAGAATGGATTGAGCAAGAGCCAC
 TGAAACTTGGACTATACCTTTGTTATTTGTATCTAAATCCAGAAGGGTCTTTGCATGTTT
 CAAATCTCAGATAGCTGGAAGGAAGAAGGACTGTTCTTTACAAGTATATAAATAGAG
 AATGAGCTAAAAAGGACCCCTCACCCCGCCGTACACACAGGAATACTATTCCAGAAA
 15 CTAGGGAGTATTTTAGTGTCTCACTATTTCCCTTTGAAAAAGTGCAATGGAAAACCTT
 ATCCATGACATACATGAGGTTGGAGTGATAAAAACAGCTGAAGGAAGAGGAAGTCTGAAA
 AAAGATGGAAACAGCAATGATGCTTGTCTATATATGTGTGACACCCACTAGTTCCCAAG
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 20 AAAGTCAATGCAAATGGATAGCAAACAAAGGGGCTATTTTTTTAAGGGACCAGAGGGTTT
 CAATCTAGAATCAGAGAAAAGATAAAAAGGGAGATGCTATAGAAAACAATAGAGAAGAT
 GTGGCCAAGAACAAGGAAAATCTCCAGTTAGCTTGGCACTTAGGGGCCAACATGTTTCTG
 TTGTTCTGGTCTTCAATACTGTATTGCATGTTGGGCTCACTATGTTTTAGTTGTGAGTGGG
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 25 CCCATTGGTAGCATCAGTGAAATTAGGAAAAAACTGTGAGCACTGCTGGCTGGACTTGGC
 AAAGTCATTCACTATTTACACATCAAATTATTAGCAACTTGAAAGTAAATCTTTGCTCAT
 CATCCAGTGGCCCCCATGATCCTGGTGAATGACTTGTAATACTGTGGAGACTGGCAACGA
 CGGTGAATTCTAGTAACACTTACCATAGAATCTGTTTCATAATTAGACTCGCCCAGATTT
 TAGTTGCTAGAGAACAATCTTTCTCCTTTACCCACATTCCTACTGAGTAGGATGCATAGG
 30 TTCGGAAACCCCATGGCATCGTTTGACTCCTCCTGGTAGTCAAGAGAGTCCAGTCACCA
 GTCTCCGAAACACCTGCCAAGTCCTAACTCCCAACAGTCTACAGTGTAACCTCAGTGTT
 TGCATGAGGTTTATGTATCTCCTTACCATTTCCTAAATGTCAATACCCGTGCACAGGATA
 TTTGCATAGGCTGCCTCCAAGCCTGGGAAACACTCTCCTCCTCGCATTGCTGGGTTTCA
 CCTTTCCAATTCAGTGTGCCCTTTAAAAGGCACTGCTTTTCTAGGCCACCCTATTGCT

GCTCACGCATGAACATCAAATCTACCACAGGCTTTTGCCTCTCAGAATTATTCTTCTTTC
 TACTATGCAATGTGGTATCCATGAGAACTTTGTCACATTGTCAAATTCTACCTTTGTTTT
 AATGnGnGCCTTTGTAATAGnGACTATGCCCAGAAATTAAATTATAGTAAGATGGGTAAC
 AACnCTTCAATTnTGGAATTTATAATTAAATAAATATTATGTAATATTATGACTTATTAT
 5 AAnGTCAATCTACTGTACCCTACTCCTACTAGGAATGCAAAGACAAATAGCAATGTGATC
 AGCATGTGCTCTTTCACAAGATCATATTGTGCATGTTGCTGATGATGCCACAGTGCATC
 TATCAGAATATCTCTGATCATTTTTTTTTTTTTTGCTTTTGAGAAGCCCCGGTTGGTGCTG
 GGATGCTTCATAGCAGGTCCACCATAGACACATGCTTAGAGGAAAGCTGCCTCTCTCTCT
 TCATTCCCAAGGAACAGTAAAAGCAGAAAAGGCTCTTATGTTCTAAAGAACAGAAAATAG
 10 CCTGCATTTCAACTACCTCCTGTTGAGAAGGCACCGAAACACACCACCAAGCAAGACACC
 CCTTTACTTTCTCCTGCTTCCCTCAATTGATGATCATTTGGAAATAAGAAGAAAGAAAA
 AGATGTGGAAGCCAATTAAAAACAGTCTTGTCTATCTCCCTGGTGAGCTCTCAACTTCTT
 AGTCAGACCAAAGTAGGTGAAAAATAATAATTTTTAATTTGGTATGAGAGTCATGTTTA
 GGCTGAAAATCTTAAAAAATCTTAGCATAAAAACATTTTCCCCTAGACCCATGAAATTTA
 15 TAATATTATCTGTGGTTGAGAAAGGCTAGTTATAGAAAAATGTTTAGAATCAGAATATTT
 TGAGGGCTCTTTTTTTGTTTTGCCTAATCATTACATTTGTTATAAGAAGTCTAAAAGTTG
 GTATGCTACAGGTCTTGTCTATTTTTCTCTGAGGTTGAGTGCCAAGTAGTCTGCATTGTG
 TTAAATCCTGCTTAAATTATCCCAAGACAATATAACTTCTCAGGAGCTAAGCCAAGGG
 CCCCTTTCAGACTACCTTAGTCCTCTCTCACCGTTGTCACCGTGGCTCATAATCAGAAT
 20 CCTGAGGGAGCATCATGAAATCTAAGGCTTTACAACAGAATCTTTCTATCCCTGGTAGAA
 ATCTTTTAACCTTGGGTTTTATTCTCATGCCATTCTGATGCTCGTATTTAAATTTTATGT
 GTTTTTTCATATGTTCTTGCATTTCTATCGTTAAATTATGGTGACATACTTTCAAATGCT
 TTGTTATTTTAAAAAGGGACAAAGAGAGATAGAAAGACAGGGAAAGATAGACAGAGGCTT
 GCCTAATACAGTCAAGAAAGAAGCTATCAAAAGTATTTAGCAATACAACATTTATGATAT
 25 ATTCATAACTGTTAACCATTTTTTAATATTCTAAAATTTCACTTTTGTTTCAGAAATGTAT
 ATTAAGAGAATCTGAGAAACATTTTTTTCTCATAGATGTAGAAAAACACACAAAATAAGG
 TATAACACATTTAAGTGATTGAAAATAAAAACAAAAGCTTGCAAACAGGAGGAAAAGTAC
 ATTGTAGGCTTTCGACATGGAGCTGCTACTAGGACCCAGGACTTGTTTATCATTTATTTG
 CCAAGTCCCACAACTCAGGGCAATACATCTCTGAGACAGTTTCCTATATTTTAATAAAA
 30 CTTCCAAAATTGATACTCAGTGTGAATTGGCTAGCTTTAATGGCAGTCATTGGATAAACA
 ATTCCAATGCCAAATTTCCCTAAGTTGATATATTTGATTAAATATGTATATTAACATCA
 GGCTATCCATCGGTTGGATCAAATACATTCTTTAGGGATCCATTCTTTTCCTTAAATTTG
 ACTTATATGTGGATTCTTTTCACAATAAATAAGTAAATGAGCATTTATTTTAAACTATT
 TTAGACGGAACTGAATTACAGCCAAGGTAGTCAAAATGACTGAGAATAATCACTTACATA

TTTACAAGGGAAAGTGACTCTTCAGATTTAAGTTTAAAATTAGAAGAGAGATAAATTTCA
CAAGCTTTCACTCCTAAGGCTAAAGATAGGCTGTGTAGGTAGTTATTTCTGAGCACATTG
GCACATCACCATTGTCAGTACTTGAGGGTTTGAATGAAGCTCACTCAAAGAACTTGGAAA
GAAGGTGGTCTTCTGACATCAATCAAGAAACAAGCTTTCCTCCCTACTTCTTCCCTAAAT
5 GCAACAACCTAAGAATTATCCACAAGATGGATGGCGCAAGGGTTCTCAATCAATTTTCAG
GATGTACATCAATGCGCAGCCTATACTACACCGAAAAGGAAGCGCATGGGTCTTAAAAAG
TAAAGGGGATATCAAAAAATTCGCAACCAAAACAAAAAGTGGCACACATTTAAGCTAGGTC
TATGTTTGGTCAGTTACACCTGGAGAAGGGGGACATTTGGTCAGCTCATTGGAACACTGT
CAAGTCCTACCAACAATTCCTCTATGCTATTACCCATTAAACCTCAGGTCTCATCGAAAA
10 AAAAAAAAAAAAA

SEQ ID NO:83

Rat T2R04 amino acid sequence

15 MLSAAEGILLCVVTSEAVLGVLGDTFIALANCMYAKNKKLSKIGFILIGLAISRIGVVW
IIILQGYMQVFFPHILTFGNITEYITYIWVFLNHLVWFATNLNILYFLKIANFSNSVFL
WLKSRVRVVFIFLSGCLLTSWLLCFPQFSKMLNNSKMYWGNTSWLQQQKNVFLINQSLTN
LGIFFFIIVSLITCFLLIVFLWRHIRQMHS DGSGLRDLNTEAHVKAMRVLISFAVLFILH
20 FVGLSIQVLCFFLPQNNLLFITGLIATCLYPCGHSIILILGNKQLKQASLKALQHLTCCE
TKRNLSVT

SEQ ID NO:84

25 Rat T2R04 nucleotide sequence

TGGTTCCATCACATGACAATAGGCTTGAAAACTTGCAGATAGAGAAGACATAACCCCTC
CAACAAGAAGCCAACATATGGGACATTCTCCAGCAGATAATTTATAACAGATGCAACGGG
AGCAACTTCGAGATCTGCAAAGATGCTGAGTGCAGCAGAAGGCATCCTCCTTTGTGTTGT
30 CACTAGTGAGGCAGTGCTGGGGGTTTTAGGAGACACATTCATTGCACTTGCAAACATGCAT
GGAGTATGCCAAGAACAAGAAGCTCTCTAAGATTGGTTTCATTCTCATTGGCTTGGCGAT
TTCCAGAATTGGTGTCTGATGGATAATAATTTTACAGGGGTATATGCAAGTATTTTTTCC
ACACATACTTACCTTTGGAAACATAACTGAATATATTACTTACATATGGGTGTTTCTCAA
TCACTTAAGTGTCTGGTTTGCTACCAACCTCAATATCCTCTACTTTCTAAAGATAGCAAA

TTTTCCAACTCTGTATTTCTCTGGCTGAAAAGTAGAGTCCGTGTGGTTTTATCTTTCT
 GTCAGGATGCTTACTTACCTCGTGGTTACTATGTTTTCCACAATTTCAAAGATGCTTAA
 CAACAGTAAAATGTACTGGGGAAACACGTCTTGGCTCCAGCAGCAGAAAAATGTCTTCCT
 TATTAACCAAAGTTTAACCAATCTGGGAATCTTCTTTTTCATTATTGTATCCCTGATTAC
 5 CTGCTTCCTGTTGATTGTTTTCTCTGGAGACACATCAGGCAAATGCACTCAGATGGTTC
 AGGACTCAGAGACCTCAACACAGAAGCTCATGTGAAAGCCATGAGAGTTCTAATATCTTT
 TCGGGTACTCTTTATCCTGCATTTTCGTAGGTCTTCCATACAAGTGCTATGCTTTTTTCT
 GCCACAAAACAACCTACTCTTTATACTGGTTTGATAGCCACATGCCTCTATCCCTGTGG
 TCACTCAATCATCTTAATTCTAGGAAACAAGCAGCTGAAGCAAGCCTCCTTGAAGGCACT
 10 GCAGCACTTAACGTGCTGTGAGACAAAAGAAATCTCTCAGTCACATAAATGGGTTTGCC
 AATTAATATCTGCCATGTTATTCCACTGATTTTTACCTGTTAGTTTCTCTGTGTCTCTGT
 TTAGTTTCTGTTTCCATGATCTGTCCATTGATGAGCGTGGGGTGTGAAATCTCCGACTA
 TTGTTGTGTGAGATGAAATGTGTGCTTTGAGCTTTAGTAAGATTTCTTTTGTGAATGTAG
 GTGCTTTTGCATTTGGTGCATAGATATTTAAGATTGAGAGTTCAGCTTGGTGGATTTTTCT
 15 CTTTGATGAATATGAAGTGTCTTGCTTATCTTTTTTGATGACTTTTGATTGAACGTCAA
 TTTTATTGGATATTAGATTGGCAACTCAAGATTGCTTCTTGAGGTCATTTGCTTGGAAG
 TTGTTTTTCAGCCATTTACTCTGAGGTAGTGTCTGTCTTTGTCTCTGAGGTGTGTTTCCT
 GCATTCAGCAAAATGCTGGGTCTCTTTACATATCCAGTTTGTAGTCTATGTCTTTTTTA
 TTGGGGAATTGAGTCCATTGATGTTGAGAGATATTAATGAATAGTGATCATTGCTTCCTG
 20 TTATTTTCGTTGTTAGATGTGGAATTATGTTTGTCTCTCTTTTGGTTTTATTGCAA
 GGAAATTATATACTTGCTTTCTGTATGGTGTAGTTTCTCTCCTTGTGTTGCAGTTTTCT
 TCTATTATCCTTTGTAGGGCTAGATTTGAAGAAAGATATTGCATAAGCTTGGTTTTGTCA
 TGGGATATCTTGGTTTCTCCATCTATGTAAATTGAGAGTTTTGCAGGATATAGTAGCCTG
 GGATGACATTTGTGTTCTCTTAGGGTCTGTATGACATCTGTCCAAAATCTTCTGGCTTTC
 25 ATAGTCTCTGGTGAGAAATCGGATGTAATTCTCATAAGTCTGCCATTATATGTCACCTTGA
 CCTTTTTCCCTTATTGCTTTTTATGTTCTTTCTTTGTTTTGTGCATTTGGTGTCTGATT
 ATTATGTGATGTGAGGTATTTCTCTTCTGGTCAAATCTATTTGGAGTTCTGTAGGCTTCT
 TGTATGTTTATGGGCATCTCTTTCTTTAGGTTATGGATGTTTTCTTCTATAAATTTGTTG
 AATATATCTACTGTCCCTTTAAGTTAGGAGCCTTCACTTTCTTCTATACCTGTTATCCTT
 30 AGGTTTAATCTTCTCACTGGATTTCTCGATGTTTTGGACTAGGAACTTTTTGCATTTTA
 CATTATCTTTGACAGGTATTTCAATGTTTTCTATGGTATCTTCTGCCACTGAGATTCTCT
 CTTCTAGCTCTTGTATAATGTTGGTGATGCTTGTACCTGTGACTCCTTGTTTCTTCCTTA
 GGTTTTCTATCTCCAGGGTGTCTCCCTTTGTGCTTTTTTTATTGCTTCTATTTCCATTC
 TAAATCCTGGATGGTTTTGTTCAATTCCTTCACCTCTTGGTTGTATTTCTGTAATTC

TTTCAGGGATTTTTGTGTTTCCTCTTTAAGGGCTTCTACTTGTTTACTTGTGTTGTCCTG
TATTTCTTTAAGGTAGTTATTTATGTCCTTCTTGAAGTCCTCCATCATTATCAAAAAATG
TGATTTTTTAAATATAAACCTTGCTTTTCTGGTGTGTTTGGATGTCAAGTATTTTCTTTGC
TGGGAGAACTGGGCTCTGATAATGCCAAGTTGTTTGATTTCTGTTGCTTAGTTTCCTGTT
5 CTTGCCTCTCGCCATTGGGTTTTCTCTGGTGTGTTGCTTATCTTGCTGTTTCTGAGAGTGG
CTTGACACTCTTGTAGGCATCTGTGTCAGGCCTCCTGTAGAACTGTTTCCCTGTTTTCTT
TCAGCCTTTTCTGAGAACAGGTGCTCTGATCTCAGGTGTGTAGGCATTCCTGGTGACTAT
CTTTCAGCTTTAGGAGCAGGCAGGAATCAGAAGGGTCCTGTCCCTGACTGCTCCTAGATC
CTTGCACCCAGGGGGCACAGTTAGCACTAGGCAATTCCTCTTGTTGTTAGGGAATGTGGGT
10 AGAGGATAGTCGCCTCTGATTTCTCAGGAATGTCTGCACTTCTGAAAGTCCAGCCCTCTC
CCCCACAGGATTTAGGTGCAGGGAGCTGTTTGACCACTTCAATTCAGTCCTGGGTGTAGA
CCAGAACCACAGGTAAAAAGAATGACTTCATTAAATTAGCAGACAAATGGGTGGAATA
GAAATGTCATCCTGGGCTGGAGAGATGGCTCAGTGGTTCAGACCACTGGCTGCTCTTCC
AGAGGTCTGAGTTCAATTCCTCAACAATAATGTTGGCTACCAACCATTACAATGAGAT
15 CAGATGCCCTCCTCTTGTGTATCTGAAGAGAGTGACAGTGTACTTACATACATAAAATAA
ATAAATAAATCTAAAAAATGTTAAAAA

SEQ ID NO:85

20 Rat T2R05 amino acid sequence

MLGAMEGVLLSVATSEALLGIVGNTFIALVNCMDCTRKNLYNIGFILTGLAISRICLVW
ILITEAYIKIFSPQLLSPINIIELISYLWIIITSQNLNVWFATSLSIFYFLKIANFSHHIFL
WLKRRINIVFAFLIGCLLMSWLFSPVVVKMVKDKKMLYINSSWQIHMKKSELIINYVFT
25 NGGVFLLFIIMLIVCFLLIISLWRHRSKWMQSNESGFRDLNTEVHVKTIKVLLSFIILFIL
HLIGITINVICLLVPENNLLFVFGLTIAFLYPCCHSLILILANSRLKRCFVRILQQLMCS
EEGKEFRNT

SEQ ID NO:86

Rat T2R05 nucleotide sequence

AAGAGATTTGAGATACTACCACAAACATTTTTTAAATATATGTAAGTCTTTAAAGAAAGA
AGGGAAAGCCACTCCTTTATTGAGCAGCCAATAGATTGCCATCTTAAATCTGTGGCAG

AAGCTATTTTAAAGATCTGCGAAGATGCTGGGTGCAATGGAAGGTGTCCTCCTTTTCAGTT
 GCAACTAGTGAGGCTTTGCTTGGCATTGTAGGGAACACATTCATTGCACTTGTGAACTGC
 ATGGACTGTACCAGGAACAAGAATCTCTATAATATTGGCTTCATTCTCACTGGCTTGGCA
 ATTTCCAGAATCTGCCTCGTGTGGATCTTAATCACAGAGGCATACATAAAAATATTCTCT
 5 CCACAGTTGCTGTCTCCTATCAACATAATTGAACTCATCAGTTATCTATGGATAATTACC
 AGTCAATTGAATGTTTGGTTTGTACCAGCCTCAGTATCTTTTATTTCCTCAAGATAGCA
 AATTTTCCCACCACATATTTCTCTGGTTAAAAAGAAGAATTAATATAGTTTTTGCCTTC
 CTGATAGGGTGCTTACTTATGTCATGGCTATTTTCTTCCCAGTAGTTGTGAAGATGGTT
 AAAGATAAAAAAATGCTGTATATAAACTCATCTTGGCAAATCCACATGAAGAAAAGTGAG
 10 TTAATCATTAACCTATGTTTTACCAATGGGGGAGTATTTTTACTTTTTATAATAATGTTA
 ATTGTATGTTTTCTCTTAATTATTTCCCTTTGGAGACACAGCAAGTGGATGCAATCAAAT
 GAATCAGGATTCAGAGATCTCAACACAGAAGTTCATGTGAAAACAATAAAAGTTTTATTA
 TCTTTTATTATCCTTTTTTATATTGCATTTAATTGGTATTACCATCAATGTCATTGTCTG
 TTAGTCCCAGAAAATAACTTGTTATTCGTGTTTGGTTTGACGATTGCATTCCTCTATCCC
 15 TGCTGCCACTCACTTATCCTAATTCTAGCAAACAGCCGGCTGAAACGATGCTTTGTAAGG
 ATACTGCAACAATTAATGTGCTCTGAGGAAGGAAAAGAATTCAGAAACACATGACAGTCT
 GGAAGACAAACAATCAGAAATAGTAAGTGAAAAAAAAAAAAAAAAAAAA

20 **SEQ ID NO:87**

Rat T2R06 amino acid sequence

EALVGILGNAFIALVNFMGWMKNRKITAIDLILSSLAMSRICLQCIILLDCIILVQYPDT
 YNRGKEMRIIDFFWTLTNHLSVWFATCLSIIFYFFKIANFFHPLFLWIKWRIDKLILRTL
 25 ACLILSLCFSLPVTENLADDFRRCVKTKERINSTLRCKLNKAGYASVKVNLNLVMLFPFS
 VSLVSFLLILSLWRHTRQMQLNVTGYNDPSTTAHVKATKAVISFLVLFIVYCLAFLIAT
 SSYFMPESLAVIWGELIALIYPSSHSFILILGNSKLKQASVRVLCRVKTMKGRKY

30 **SEQ ID NO:88**

Rat T2R06 nucleotide sequence

GTGAGGCCTTAGTAGGAATCTTAGGAAATGCATTCATTGCATTGGTAAACTTCATGGGCT
 GGATGAAGAATAGGAAGATCACTGCTATTGATTTAATCCTCTCAAGTCTGGCTATGTCCA

GGATTTGTCTACAGTGTATAATTCTATTAGATTGTATTATATTGGTGCAGTATCCAGACA
 CTTACAACAGGGGTAAAGAAATGAGGATCATTGATTTCTTCTGGACGCTTACCAACCATT
 TAAGTGTCTGGTTTGCCACCTGCCTCAGCATTTTCTATTTCTTCAAGATAGCAAACCTTCT
 TCCATCCTCTTTTCTCTGGATAAAGTGGAGAATTGACAAGCTAATTCTGAGGACTCTAC
 5 TGGCATGCTTGATTCTCTCCCTATGCTTTAGCCTCCCAGTCACTGAGAATTTGGCTGATG
 ATTTTCAACGCTGTGTCAAGACAAAAGAAAGAATAAACTCTACTCTGAGGTGCAAATTAA
 ATAAAGCTGGATATGCTTCTGTCAAGGTAAATCTCAACTTGGTCATGCTGTTCCCTTTT
 CTGTGTCCCTTGTCTCATTCTTCTCTTGATTCTCTCCCTATGGAGACACACCAGGCAGA
 TGCAACTCAATGTAACAGGGTACAATGATCCCAGCACAAACAGCTCATGTGAAAGCCACAA
 10 AAGCAGTAATTTCTTCTAGTTCTGTTTATTGTCTACTGCCTGGCCTTTCTTATAGCCA
 CTTCCAGCTACTTTATGCCAGAGAGTGAATTAGCTGTAATTTGGGGTGAGCTGATAGCTC
 TAATATATCCCTCAAGCCATTCATTTATCCTGATCCTTGGGAACAGTAACTAAAACAGG
 CATCTGTAAGGGTGCTTTGTAGAGTAAAGACTATGTTAAAGGGAAGAAAATATTAGCATC
 ATGGATATATTTGAAGAAAACTATCACTGTCTAAAGAAAAAGGATGACAAATCATTATC
 15 TTTCATTCTTATATGAATATTGCTTTCATGCGGTAAACATCTTTTAACAACTTAAATCAA
 ATGTTGGGAAATCTCATATACAGCAACTTTGCATGTCTCTCTGTCTATTTCCCTCTCCCT
 TTGTACATAGTTGACATAAAAAAAGAATTTTCATGACAAAATTGTAATAAATAGCTACAG
 AGGCAGCACATTTTCATAGTAAGTTCTGAATCACTCTTCCAAATGCAAAGCTGCCTGACA
 AATTCAAACAACCTGTAACAGTATTTCACTGCTGTTTGCATTCTTTGGAAAAGCAGGTGG
 20 TTTGTTCCCTATGACCTGACTTGGAGTTTTCTTCTTACATCACTG

SEQ ID NO:89

Rat T2R07 amino acid sequence

25 MGSSLYDILTIVMIAEFIFGNVTNGFIVLTNCIAWLSKRTLFIGWIQLFLAISRVVLIW
 EMLLAWLKYMKYSFSYLAGTELRVMMMLTWVVSNHFSLWLATILSIFYLLKIASFSRPVFL
 YLKWRVKVLLLLILLGNLIFLMFNILQINTHIEDWMDQYKRNITWDSRVNEFVGFSNLVL
 LEMIMFSVTPFTVALVSFILLIFSLWKHLQKMHLSRGERDPSTKAHVNALRIMVSFLLL
 30 YATYFISFFISLIPMAHKKGLDLMFSLTVGLFYPPSSHFILILGHSNLRHSSCLVITYLR
 CKEKD

SEQ ID NO:90

Rat T2R07 nucleotide sequence

CAGTAGCAAAATTTTACTATGTTTCATTGATATTATGTCAnGnCACTACGTAAGAAGGAAG
 ACTTGAAAGAAAGCTTATCTGAGTTTTTAAGAATACATGGACATTTTCAGCTTGGCAAATG
 5 ACGAGCTGTGAATTTTTGTCATCTGGACATGGGAAGCAGCCTGTATGATATCTTAACTAT
 TGTCATGATTGCAGAGTTTATATTCGGAAATGTGACCAATGGATTCATAGTGCTGACAAA
 CTGTATTGCTTGGCTCAGTAAAGAACTCTTTCTTTTCATTGGTTGGATCCAGCTTTTCTT
 GGCCATTTCCAGAGTGGTTTTGATATGGGAAATGTTACTAGCATGGCTGAAATATATGAA
 GTATTCATTTTCATATTTGGCTGGCACAGAATTAAGGGTTATGATGTTGACCTGGGTAGT
 10 TTCCAATCACTTTAGTCTCTGGCTTGCCACCATTCTAAGCATCTTTTATTTGCTCAAAAT
 AGCTAGTTTCTCCAGACCTGTTTTCTGTATCTGAAGTGGAGAGTAAAAAAGTGCTCCT
 GCTGATTCTTCTCGGAAATTTAATCTTCCTGATGTTCAATATATTACAAATCAACACTCA
 CATAGAAGACTGGATGGATCAATATAAGAGAAATATAACGTGGGATTCCAGAGTGAATGA
 ATTTGTGGGGTTTTCAAATCTGGTTTTATTGGAGATGATTATGTTCTCTGTAACACCATT
 15 CACCGTGGCTCTGGTCTCCTTCATCCTGTTAATCTTCTCTTTATGGAACATCTCCAGAA
 GATGCATCTCAGTTCAGAGGGGAACGAGACCCTAGCACAAAAGCCCATGTGAATGCCCT
 GAGAATTATGGTCTCCTTCCTCTTACTCTATGCCACTTACTTCATATCCTTTTTTATATC
 ATTAATTCCTATGGCACATAAAAAAGGACTAGATCTTATGTTTAGCCTAACTGTTGGACT
 TTTCTACCCTTCAAGCCACTCATTTATCTTGATTTTGGGACATTCTAATCTAAGGCATTCT
 20 CAGTTGTCTGGTGATAACCTATCTGAGATGTAAGGAAAAGGATTAGAAATTCATATTCC
 ATAAGGCAGTTAAACCACATGCTATTAGGTATACTCAGTGCTAGATCCCTAGGCAAGCAT
 TAACATTAAAAATATATAATTTCTAGATTCTTCTATTTGTGATAAACCACTCACTTAGAA
 TAATGCTAAAGTAGCGTGATGTTGTATATAAGTGTAAGAATAAAATGTAATTAATTTAGT
 TTAGGCACAATAACATATGTCTACTAAGTAAAACTAGGCAGGCTGCTACACGCATATTA
 25 GAATCCAGGCTGAGGTATATAGACTCAAGAAATACTGTGGAATAAAGATTTTAATTTTCA
 TTCTATTGTGAGTTATGTGAAATCAATGCCATTAAAGGCATACACAAGATTTTACACAC
 TGAAACAACCTTCTTGCATTTTGTTCATATTGTATTGGAAGTAAATTGGAGATAAACTTAAT
 ATCAATAAATTACAAAATGTAAACATAAACAGGGTGATTAAAAATTAGCCTCTAGGTCCT
 GGGGAAATGATTCaAGTAAAGTGCTTTCTTTTCAAATAGGAGAATCTGATTGTAAATCAT
 30 CTAAAAGTCTGGCATAAAATGTCAATGAAAATTGTATGTAAAATATAGCTATgGCmAAGA
 GCACCmAAGAAAAGAAAATTTTTGCCTTTGAAACCCAGTAATTGATATCCTTTAAAAAAG
 CAGTTACATATTTTTCTGTTTAAGATTTTGTCAAAGGGTAGCTTTGACAACTAATATAAG
 CTGAGGAAGGTAGCAAGTGTGAAGTCAGCTAATGGGGTCAGTCAAGTGCTGTTAGCAGCA
 GATGGAGGCCACTGCTGAATTTAGCAGGCAATTTACAGGGTGAGCACTGCTAGTGCTGAC

AGAAGAAAACTCTGAAATTTTAACTCTTTAGGGTCTGGTGAGAAAGAAAAAGAGAGAAA
ATCGCATA
TCATGGAAGCTCTAACAAGTTGACTCAAACAACCTTTATGATGTTTTTAGGCCCTTTTATT
TTAATGTCAGTGAATTAGGTGTGGTACAGCAATATTGCTACTTTTAAATTCAAAGCAGT
5 GTTTTATATATTATTCATTATATAAGCTAATTATAAGTTTAAATCAAAGGTTTATTTGT
CCATGATTTTACTTTATCATTGGGCACACCTGTGCTCTCATCCTTGGGCTTGACCTAGAA
TGAAAGTTTATCCTTGATCATATGTCTGTACAAGACTACTTCTCTTCCCTATAGTAGTTT
ATGTACTTACAATATACAAAAGTTTATTGAATTCCTTTTATCACTTATGCAGCCTTTTCT
TACTATTCTATTCTATTCTATTCTATTCTATTCTATTCTATTCTATTCTATTCTATTCTA
10 TTCTATTCTATTCTATTCTAGAACTAACCTATACATTCATTTCTGGCAAAACAACCTTAT
ATCATCTCCTTAATTATTTTATCAATTAATCTAACATCCTGAAGTTATTTAAATCTAATA
TAAGGACTCTGTAAAGTCACAAATTTATTTATACTTCACAAAATTCATTATTTTATGGAA
CTGCAGCATTGCCTGGGCCAGGAGTCACAAGAGTTCCAGAGTTGACTTTATTGGCATCTG
CCTGGCTAACTGAAGGATCAGTTTTCTGTGTACAATAATTTTGTGTATCTCTTTTGATGC
15 AAGATATGAAAAATAATTTTCACTCTAAAAGTGTCTTAAATTTGAAACTCTCTGGCCAGA
ATCTAACTATTGATGACCAGTTTGCACCATGGACTCAGTGTCTTCTATTGCTTTAAATA
AGCAACATCTTGAATGCTTTTCTTGTGTATTAGGCAAATAATTAACAACATGTTTCTATG
ATTGTCTCAATAACAATACTATATTTCTCACAGTTTTTAATTTTTTATGGCAAAGTTGGCT
AATAAGAATTTTTTTCAAATTATCAAACGTGAAGAAAACCTGACATTTTATTTTCATGGAG
20 ATTCTAAATGTTTTCTTAGCATATTGCCTTTTTACTAACTTGATTTTTATCATGTTTTGG
TAGTATTTCTAATTTTCCTTTTTTTCTAAGTATGTTATGTAGTAACACCAGGAGAATGAA
ACAAATGACATTTATACTAAGGATGTGACAAATAAGGCCCAAAGAAAGTTTTGAAAATCA
TGATCTCATTCTATTCTTCTTTATTAAGTATAGCATAAGCAAATTCCTGATGGTGGTCT
TGGCCCATATCTTTGAACACAGTGTAGTGGTGAAGACTTTTTCAAATATTATGTCATATT
25 TGTACCCATCTCTGTACCTATTTCTTCTGATTTTCATGAGGAAAAAATGAGGAAGGGTTTG
TTTGTGTGCTGGAGCAGCTGAAGTGGACCAAGGGGCAGGAATTCTCTCTGTTCCGGTCCTA
GTGTGACTGATGATGCTCTCATTGAAAAACAGGAAGAAGAAGAAAGACTTTATATGCACC
ATTCACTCCTTCCCCCTCCTACATTCCACCTCCCTCTTGAAAGAGTGTCTATCTATATAG
ATATAGCTATCCTGAAATCCATTAAGTAGACCTGACTGGCTTAAATCTCACAGAAATTCA
30 CCTACCTTTTCCATGATTGCTGAAATTAAAGACATGTGCCGACATATTGGGCACATTCAG
ACCTTTTGCCAACTGTCTTCAACTCATTGGACCTACTGAGAAGTATTCAAATATTTG
GTTGTTTTAAATAAAAGGAAAGTGGGTCTATATTACTTGAATTGGATAGAGAAATTTTCA
CTTACAAGTGATATTGAAAATGGGGGAGAATGTATTTTAGCATAAGCACCAGAACACAAA

GCAATTCTTGTTAAACTTTATCGATAAATTGGATAAATGTTAAAAAGAAAAATAAAA
TATACGAAC TATTATGAAAAAAAAAAAAAAAAAAAA

5 **SEQ ID NO:91**

Rat T2R08 amino acid sequence

MEPVIHVFATLLIHVEFIFGNLSNGLIVLSNFWDWVVKRLSTIDKILLTLAISRITLIW
EMYACFKIVYGSSSFIFGMKLQILYFAWILSSHFSWLFATALSIFYLLRIANCSWKIFLY
10 LKWRLKQVIVGMLLASLVFLPGILMQRTLEERPQYGGNTSEDSMETDFAKFTELILFNM
TIFSVIPFSLALISFLLLI FSLWKHLQKMLSSRGHGD PSTKAHRNALRIMVSFLLLYTS
YFLSLLISWIAQKHHSKLVDIIGIITELMYPVSHSFILILGNSKLKQTSWILSHLKCRL
KGENILTPSGKPIN

15

SEQ ID NO:92

Rat T2R08 nucleotide sequence

CTGCAGGTTGGTGATCCAGTAATGAGCAGCACTGTTATATCTCAGGCTTTCTAAGATCAT
20 **GGAACCTGTCATTCACGTCTTTGCCACTCTACTAATACATGTGGAGTTCATTTTTGGGAA**
TCTGAGCAATGGATTAATAGTGTGTCAAACCTTCTGGGACTGGGTCGTTAAACGAAAAC
TTCCACAATTGATAAAATTCTTCTTACATTGGCAATTTCAAGAATCACTCTCATCTGGGA
AATGTATGCTTGTTTTAAATTGTATATGGTTCATCTTCATTTATATTTGGGATGAAGTT
ACAAATTCTTTATTTTGCCTGGATCCTTTCTAGTCACTTCAGCCTCTGGTTTGCCACAGC
25 **TCTCAGCATCTTTTACTTACTCAGAATAGCTAACTGCTCCTGGAAGATCTTCCTGTATCT**
GAAATGGAGACTTAAACAAGTGATTGTGGGGATGTTGCTGGCAAGCTTGGTGTTCTTGCC
TGGAATCCTGATGCAAAGGACTCTTGAAGAGAGGCCCTATCAATATGGAGGAAACACAAG
TGAGGATTCCATGGAAACTGACTTTGCAAAGTTTACAGAGCTGATTCTTTTCAACATGAC
TATATTCTCTGTAATACCATTTTCATTGGCCTTGATTTCTTTTCTCCTGCTAATCTTCTC
30 **TTTGTGGAAACATCTCCAGAAGATGCAGCTCAGTTCAGAGGACATGGAGACCCTAGCAC**
CAAGGCCACAGAAATGCTTTGAGAATTATGGTCTCCTTCCTCTTGCTCTACACTTCATA
TTTCTGTCTCTTCTTATATCATGGATTGCTCAGAAGCATCACAGTAACTGGTTGACAT
TATTGGTATTATTACTGAACTCATGTATCCTTCAGTCCACTCATTTATCCTGATTCTAGG
AAATTCTAAATTAAAGCAGACTTCTCTTTGGATACTGAGTCATTTGAAATGTAGACTGAA

AGGAGAGAATATTTTAACTCCATCTGGCAAACCAATTAAGCTGTTATATATTCTGTA
 TTGCAAACAAATCAGTGAGTTAGTGGTTCAAGGATTCCATCCTTGACTTATTGTATCATG
 GAAGTCATATAGGGAGAGGCTGAACAAGCTATCTTCTGTAAATTGGCAAGGGTTGCATAT
 AGTACTGGTACTGGGACACCATCCAACCATAAAACCTTCTAACCATAACCTACCTGACTG
 5 CAAGATATGCTGGGACAATGGTGGCTCAGAGATTTTGGGACTGGCCAACCAATGTCTATT
 CTTTCTTGAGGCTCACTCAATAAGGAGGCCATGCCCAACTCGTCcTGGATGGCCAGGAAC
 CAGAATCTCTGATGGsCCAATGATCTATGGnAGAACCAGCATTACTGGGAAAAAAGAAT
 AATCACTTTGATGAATGGTCAAATATTTCTAAATATATTCTGATACACTTGTACATCAT
 TTCTCTTTCCCAATCATCATCACAGGGACTTCTCCCCAGCACCTGATGGGAACAGATACC
 10 AAAATCTACAGCCAAATACTAAATGCAGGTTGGGGAACCTCCACAAAAGACTGGAAGGAAG
 TACTGTGAGAGCCAGAGTGGTCCAGAACACTAGGAGAACACAGAACATCGAATTAATAA
 GCAGCACTCATAGGGTTAATGTAAAATAAAGCAGCAGTCACATAGACTGCACAGGTGTAC
 TCTAGATCCTCTGCATATATGTTGTGGTTGTCAAACCTGGGAGTTTTGTTGGACTAATAA
 CAATGTGAATAAGTAAGTCTCTGACACTTATTCCCGCTCTTGGAACCCTTTTCCACATTT
 15 TGTATTGTCTTACCACCTTGATATGAAGGTTTCTGAATAGTCCAAAAAAAAAAAAAAAAAA
 AAAAAAAAAAAAAAAAAAAAAAAAAA

SEQ ID NO:93

20 Rat T2R09 amino acid sequence

MLSAAEGILLSIATVEAGLGVLGNTFIALVNCMDWAKNKKLSKIGFLLFGLATSRI FIVW
 ILILDAYAKLFFPGKYLSKSLTEIISCIWMTVNHMTVWFATSLSIFYFLKIANFSHYIFL
 WLKRRTDKVFALLWCLLISWAISFSFTVKVMKSNPKNHGNRTSGTHWEKREFTSNYVLI
 25 NIGVISLLIMTLTACFLLIISLWKHSRQM QSNVSGFRDLNTEAHVKAIFLISFIILFIL
 YFIGVAVEIICMFIPENKLLFIFGLTTASVYPCCHSVILITNSQLKQAFVKVLEGLKFS
 ENGKDLRAT

30 **SEQ ID NO:94**

Rat T2R09 nucleotide sequence

GGCACTGCAGCAGATCTGCTATAGAATAACAGATACAAACATAGCAACCTGCAGAG**ATG**
CTCAGTGCAGCAGAAGGCATCCTTCTTTCCATTGCAACTGTTGAAGCTGGGCTGGGAGTT

TTAGGGAACACATTTATCGCCCTGGTTAACTGCATGGATTGGGCCAAGAACAAGAAGCTC
 TCTAAGATTGGTTTCCTTCTCTTTGGCTTAGCAACTTCCAGAATTTTTATTGTATGGATA
 TTAATTTTAGACGCATATGCAAAGCTATTCTTTCCGGGAAGTATTTGTCTAAGAGTCTG
 ACTGAAATCATCTCTTGTATATGGATGACTGTGAATCACATGACTGTCTGGTTTGCCACC
 5 AGCCTCAGCATCTTCTATTTCTAAAAATAGCAAATTTTTCCCACTATATATTTCTCTGG
 TTAAAGAGGAGAACTGATAAAGTATTTGCCTTTCTCTTGTGGTGTATTATTAATTTTCATGG
 GCAATCTCCTTCTCATTCACTGTGAAAGTGATGAAGAGCAATCCAAAGAATCATGGAAAC
 AGGACCAGTGGGACACATTGGGAGAAGAGAGAATTACAAAGTAACTATGTTTTAATCAAT
 ATTGGAGTCATTTCTCTCTTGATCATGACCTTAACTGCATGTTTCTTGTTAATTATTTCA
 10 CTTTGGAAACACAGCAGGCAGATGCAGTCTAATGTTTCAGGATTCAGAGATCTCAACACT
 GAAGCTCATGTGAAAGCCATAAAATTTTTAATTTTCATTTATCATCCTTTTCATCTTGTAC
 TTTATAGGTGTTGCAGTAGAAATCATCTGCATGTTTATCCCAGAAAACAACTGCTATTT
 ATTTTTGGTTTGACAACTGCATCCGTCTATCCCTGCTGTCACTCAGTCATTCTAATTCTA
 ACAACAGCCAGCTGAAGCAAGCCTTTGTAAAGGTACTGGAGGGATTAAAGTTCTCTGAG
 15 AACGGAAAAGATCTCAGGGCCACATGAGTCTGGAACAGAAATGGGTAGTCTGGAATAATT
 GTAAGGAAGTCGTAGAAGGTCTTTTTTCATTTGTACAGTGCTCTTACCTTGTTTTTGAGGA
 GATGTAAACTTTTTTATTTTTATTTTTTATCCTATGTGAATAAGTGTGTGTGTGTGTGTG
 TGTGTTTATGTGTGTGTGTATATATGTCTATGTGTGTTTTAGGAGGTTTAAGAGGGAAGA
 GGAATAGAGGTATGTTGGTGTTTTTAACATGGATATTCACAGGCCAAGGAACCTGTTCT
 20 CTCCTTTTACCTTAGGGTAGTGTCTTTGTGGCTGTCACTCTGACAGTCTACACTAGTTG
 AACTAAGAGCTTTTAGCCAGTTCACCTTGTCTAAACCTCCCTTCTCATGGTAGCAGTGTTT
 TGATTACAGAATCATGCTGTACATACAGCTTTTTTAACAAGGTTCCCATAGACAGAATTC
 ATGTCAAACGGAATGCACAGCTGTCACTCTTACCCACCGATCTCTCTTGCCAGCCCATTCT
 CTATTGACTTTTAACTGTAGTATTAACTTTACTGAAATCTTCTGCAACCAGTCTGACTA
 25 TGTCTCTTGAAATCACATGATATGGTGGAAATTTAATGCCATGTGAAAATTTGTTTGTTT
 AGTTAGTTTTCCTACTCTGCCAAATCATTCTCTTACACTTGGCAGAAAAAACCATCAACT
 GTAGACTATTTTGTGTAAAGACTAATACAGATAGAATAAGTATCTTAATCAAGATGTCAT
 TGTGATTATCCTAATTTCCCCAGAGCACTGGTTCCCTTTCCCCAGAAAGACTCACAAAGG
 AACTGAGGCAAACAGTTGTGGTCACTCTTGATATTTACCAGTTGAAACTGAAGAACAGTG
 30 TTTCTTTCTGTTTCAGTTTACTACTTACAGTTACTTTATTTTCATCCATTAAATCCCAAA
 GTGCTTATTAATAGTAGATATTTGATGAAGCAACAATGGTTATAAGAGTGGATGTGGATC
 TATGACAAAGATCTAGAGAAACAGACTATTTGTGAAAGATGGATGAAAGCCCTGATGAAA
 GGATTCTTCATGGTCTTTGACCCAGGGAGTTTTGAAATCAAGCAGCCACAGATCAAAGA
 GAGCTGAGAAGAGGTTCTCCTGAAGAAAATATCCAAACACATGGTGCCAGCCAAAGCAGA

AAATAGTGGACAATTCAGTCCAGGACCTGAATGAGGTAGACAATGTCCTGTTAAGGGTTG
 GAACAAATATATAGATATGGTCATTCATATACAGAAACCTACAGGCGTGTTTGAACCTT
 GGTTTCTCAGTAATCAATTCTTAAATCTTTTTTTAGAATGGATTTTTTATCATCATTCATG
 ATCTCTCAGCAGAGTCTGCAGGGGCTAAGAGACACACTAAGAGTATCTGGAGGGGGGAGT
 5 GTCTTCCTGCTCTATCAACCCCTAAAGTCATATATAACAATACAAAATTCCACATTAGTT
 AAGTTCTTTTTTTTACATCTTTATTAAATTGGGTATTTCTTATTTACATTTCAAATGTGA
 TTCCCTTTCCTGGTTTCCAGGCCAATATCCCCCTAACCTCTCCCCTTCTATGTGGGTATT
 CCCTCGTGCCGAATTC

10

SEQ ID NO:95

Rat T2R10 amino acid sequence

MFLHTIKQRDIFTLIIFFVEITMGILGNGFIALVNIVDWIKRRRISSVDKILTTLALTR
 15 LIYAWSMLIFILLFILGPHLIMRSEILTSMGVIWVVNNHFSIWLATCLGVFYFLKIANFS
 NSLFLYLKWRVKVVL

SEQ ID NO:96

20 Rat T2R10 nucleotide sequence

CCCGGGCTGCAGGATTCGGCACGAGAATGAAACTTTTGCTCTACTATTTTGCTGTTCTG
 TGATACCACAGACCATAAAACAATCGAGCCAAGGGATCAAGAGCTGAAACTTCAGAAAGT
 GGGAATCAAATTTCTTCCTGATAGGTTAGCTTATGAGAATTCAGCATCTTATTCAACTT
 25 CAGAAAATTGGATATAAGATACAGTGTCTGGATGAAGCCGAATTGATCTATTTGGGGAGA
 AAAACGCCAACATTTATAATAAGGTTTTATGAGACAGTTCCTGGGAAATTTGGATATTT
 CCTAGTTAGTAATGTGTAAATGGGATTTTAAAACATGATTATTTTGTATTTTAAACAACC
 AACATGAGGAGCTTTTTAAATGCCACTTAGACATTATAAACTGAAGC**ATGTTCTTACACA**
CAATAAAGCAACGTGATATTTTACTTTGATAATCATATTTTTTGTGGAAATAACAATGG
 30 **GAATCTTAGGAAATGGATTCATAGCACTAGTGAACATTGTGGACTGGATCAAGAGAAGAA**
GGATTTCTTCAGTGGATAAGATTCTCACTACCTTGCCCTTACCAGACTCATTTATGCGT
GGTCTATGCTCATTTTTATATTGTTATTCATACTGGGCCCGCATTGATTATGAGATCAG
AAATACTTACATCAATGGGTGTTATCTGGGTGGTGAACAATCACTTCAGCATCTGGCTTG

**CTACATGCCTCGGTGTCTTTTATTTTCTCAAGATAGCCAATTTTCTAACTCTTTGTTTC
TTTACCTAAAGTGGAGAGTTAAAAAGTGGTTTAAATG**

5 **SEQ ID NO:97**

Rat T2R11 amino acid sequence

GSGNGFIVSVNGSHWFKSKKISLSDFIITSLALFRIFLLWIIIFTDSLIIIVFSYHAHDSGI
RMQLIDVFWTFTTHFSIWLLISCLSVFYCLKIATFSHPSFL*LKSR

10

SEQ ID NO:98

Rat T2R11 nucleotide sequence

15 GGATCCGGAAACGGTTTTATCGTGTCAGTCAATGGCAGCCATTGGTTCAAGAGCAAGAAG
ATTTCTTTGTCTGACTTCATCATTACCAGCTTGGCCCTCTTCAGGATCTTTCTGCTGTGG
ATCATCTTTACTGATAGCCTCATAATAGTGTTCTCTTACCACGCCCACGACTCAGGGATA
AGGATGCAACTTATTGATGTTTTCTGGACATTTACAACCCACTTCAGTATTTGGCTTATC
TCCTGTCTCAGTGTTTTCTACTGCCTGAAAATAGCCACTTTCTCCCACCCCTCATTCCTG
20 TAGCTCAAATCTAGA

SEQ ID NO:99

Rat T2R12 amino acid sequence

25

MLSTVSVFFMSIFVLLCFLGILANGFIVLMLSREWLWRGRLLPSDMILLSLGTSRFCQQC
VGLVNSFYYSLHLVEYSRSLARQLISLHMDFLNSATFWFGTWLSVLFCIKIANFSHPAFL
WLKWRFPALVPWLLLGSILVSFIVTLMFFWGNHTVYQAFLLRRKFSGNTTFKEWNRRLRID
YFMPLKLVTTIPCSLFLVSILLINSLRRHSQRMQHNAHSLQDPNTQAHSRALKSLISF
30 LVLYALSYVSMVIDATVVISSDNVWYWPWQIILYLCMSVHPFILITNNLKFRGTFRQLLL
LARGFWVT

SEQ ID NO:100

Rat T2R12 nucleotide sequence

GTGTGAGGGACTGTGGGTAGGGGCTGGGAGGAGGCCAGGAACCAAGGCAACCAGTGGTGA
CAGGAGGGGCTGAAATGCTATCAACTGTATCAGTTTTCTTCATGTCGATCTTTGTTCTGC
5 TCTGTTTCCTGGGAATCCTGGCAAACGGCTTCATTGTGCTGATGCTGAGCAGGGAATGGC
TATGGCGCGGTAGGCTGCTCCCCCTCAGACATGATCCTCCTCAGTTTGGGCACCTCCCGAT
TCTGCCAGCAGTGC GTTGGGCTGGTGAACAGTTTCTACTATTCCCTCCACCTTGTTGAGT
ACTCCAGGAGCCTTGCCCGTCAACTCATTAGTCTTCACATGGACTTCTTGAACCTCAGCCA
CTTTCTGGTTTGGCACCTGGCTCAGCGTCCTGTTCTGTATCAAGATTGCTAACTTCTCCC
10 ATCCTGCCTTCCTGTGGTTGAAGTGGAGATTCCCAGCATTGGTGCCTTGGCTCCTACTGG
GCTCTATCTTGGTGTCTTCATCGTAACTCTGATGTTCTTTTGGGGAAACCACACTGTCT
ATCAGGCATTCTTAAGGAGAAAGTTTTCTGGGAACACAACCTTTAAGGAGTGGAACAGAA
GGCTGGAAATAGACTATTTTCATGCCTCTGAAACTTGTCAACCACGTCAATTCCTTGCTCTC
TTTTTCTAGTCTCAATTTTGCTGTTGATCAATTCTCTCAGAAGGCATTACAAAGAATGC
15 AGCACAATGCTCACAGCTTGCAAGACCCCAACACCAGGCTCACAGCAGAGCCCTGAAGT
CACTCATCTCATTTCTGGTTCTTTACGCGCTGTCCTATGTGTCCATGGTCATTGACGCTA
CAGTTGTCATCTCCTCAGATAACGTGTGGTATTGGCCCTGGCAAATTATACTTTACTTGT
GCATGTCCGTACATCCATTTATCCTTATCACTAATAATCTCAAGTTCCGAGGCACCTTCA
GGCAGCTACTCCTGTTGGCCAGGGGATTCTGGGTGACCTAGAAGGTTTGGTCTCTTTATC
20 TGTACCCTTTGAAGAGACTTAGGTGAGGGTGACTTCCCTTGGAAGTGATCTCATCTACAT
GGAAATGTCTTTGTAGGCTGACATGGGGTCATACTATGTGGTTCCTCCTTGGGAAAGAGG
AGAAGAAAATACAGGGATTCTGAGCGTTCTTCCTTATCTTGGGATATTATGAAAATGGAC
ATTCTGAATCCTGAACCAGTATTGATCTGAAGTGCAAAGTACAATATGCCTGTTCCCTTC
ATGTCTGCTATCCTCTTGGTACTTATTAATTCCCT

25

SEQ ID NO:101

Rat T2R13 amino acid sequence

30 MCGFPLSIQLLTGLVQMYVILIIAVFTPGMLGNVFIGLVNYSWVKNKKITFINFILICL
AASRISSVLVVFIDAIILELTPHVVHSYSRVKCSDFWVITDQLSTWLATCLSIFYLLKI
AHFSHPLFLWLKWRLRGVLVGFLLFSLFSLIVYFLLLELLSIWGDYVIPKSNLTLYSET
IKTLAFQKIIIVFDMLYLVPFLVSLASLLLLFLSLVKHSQNLDRISTTSEDSRAKIHKKAM

KMLLSFLVLFIHIFCMQLSRWLFFLFPNNRSTNLLLLTLNIFPLSHTFIIILGNSKLRQ
RAMRVLQHLKSQQLQELILSLHRLSRVFTMEIA

5 **SEQ ID NO:102**

Rat T2R13 nucleotide sequence

GGGATTTCAGTTGGATAAGAGAAAAGTCAAAACCCTAAGACTAAGAATTTCTTAAGTAGA
TATCAATTTCTATCCATTGGAAGGAGTTTCCAATCACACTGAAATTACAATAAAAAAGGA
10 GCAAGATAACTATGGGAAGGATGATTTTCGGTGGATGTTTGAGAACTGAGCAGCAAGGC
AAATTGATAGATGTGTGGATTCCCTCTTTCTATTCAACTGCTTACTGGATTGGTTCAAAAT
GTACGTGATATTGATAATAGCAGTGTTTACACCTGGAATGCTGGGGAATGTGTTTCATTGG
ACTGGTAACTACTCTGACTGGGTAAAAACAAGAAAATCACCTTCATCAACTTCATCCT
GATCTGTTTGGCAGCGTCCAGAATCAGCTCTGTGTTGGTGGTATTTATTGATGCAATCAT
15 CCTAGAACTAACTCCTCATGTCTATCATTCTTACAGTCGAGTGAAATGCTCTGATATATT
CTGGGTATAACTGACCAGCTGTCAACGTGGCTTGCCACCTGCCTCAGCATTTTCTACTT
ACTCAAAATAGCCCACTTCTCCCATCCCCTTTTCCTTTGGTTGAAGTGGAGATTGAGAGG
AGTGCTTGTTGGTTTTCTTCTATTTTCTTTGTTCTCATTGATTGTTTATTTTCTACTCCT
GGAATTACTGTCTATTTGGGGAGATATTTATGTGATCCCTAAAAGCAATCTGACTTTATA
20 TTCAGAAACAATTAAGACCCTTGCTTTTCAAAGATAATTGTTTTTGATATGCTATATTT
AGTCCCATTCTTGTTGTCCCTAGCCTCATTGCTCCTTTTATTTTTATCCTTGGTGAAGCA
CTCCCAAACCTTGACAGGATTCTACCACCTCTGAAGATTCCAGAGCCAAGATCCACAA
GAAGGCCATGAAAATGCTATTATCTTTCCTCGTTCTCTTTATAATTACATTTTTTGCAT
GCAGTTGTCACGGTGGTTATTCTTTTTGTTTCCAAACAACAGGTCAACTAATTTTCTTTT
25 GTTAACATTAAACATCTTCCATTATCTCATACTCATTATCATCCTGGGAAACAGCAA
GCTTCGACAAAGAGCAATGAGGGTCCTGCAACATCTTAAAGCCAACTTCAAGAGTTGAT
CCTCTCCCTTCATAGATTGTCCAGAGTCTTCACTATGGAAATAGCTTAAAGGGGAGACTT
GGAAGGTCACCTGGTAACTTGTTCTTCCGCTGAGTTCTGTTAAGTAATGCTGGACATATAT
GAACTATCCCTAGTGCATACTGATATT

30

SEQ ID NO:103

Rat T2R14 amino acid sequence

VANIMDWVKRRKLSAVDQLLTVLAI SRITLLWSLYILKSTFSMVPNF EVAIPSTRLTNLV
WIISNHFN

5 **SEQ ID NO:104**

Rat T2R14 nucleotide sequence

CTGTGGCAAACATAATGGATTGGGTCAAGAGAAGGAAGCTCTCTGCAGTGGATCAGCTCC
TCACTGTGCTGGCCATCTCCAGAATCACTCTGTTGTGGTCATTGTACATACTGAAATCAA
10 CATTTTCAATGGTGCCAACTTTGAGGTAGCTATACCGTCAACAAGACTAACTAATCTTG
TCTGGATAATTTCTAACCATTTTAAT

SEQ ID NO:105

15 Mouse T2R01 amino acid sequence

MQHLLKTIFVICHSTLAIILIFELIIGILGNGFMALVHCMDWVKRKKMSLVN KILTALAI
SRIFHLSLLLISLVIFFSYSDIPMTSRMTQVSNNVWIIIVNHFSIWLSTCLSVLYFLKISN
FSNSFFLYLKWRVEKVSVTLLVSLLLLILNILLINLEISICIKECQRNISC SFSSHYYA
20 KCHRQVIRLHIIFLSVPVVLSTFLLLI FSLWTLHQRMQQHVQGGRDARTTAHF KALQT
VIAFFLLYSIFILSVLIQNELLKKNLFVVFCEVVYIAFPTFHSYILIVGDMKLRQACLPL
CIIAAEIQTTLCRNFRSLKYFRLCCIF

25 **SEQ ID NO:106**

Mouse T2R01 nucleotide sequence

AGCTGTGCGTGAGCAAAGCATTTCTTGTCTGCCACTTCTGAGCTGTGTGAGGAGACACAT
TATCACGGAAAGAGATT CAGACTCTGTGCTGTCAAACCTGTATGTTTGCTCCTCTTTTA
30 CTGTGAAGGCAGAGTTACGAAAAAAATGTTATGAGAACCAACTCAGAAATTGACAAAAA
TTTTCTAAATGTCATTTTTTAAAATTATATTTCAAATGGAAATGTGAGCAAATCTTTATA
ACTAATATATAAAATGCAGCATCTTTTAAAGACAATATTTGTTATCTGCCATAGCACACT
TGCAATCATTTTAATCTTTGAATTAATAATTGGAATTTTAGGAAATGGGTT CATGGCCCT
GGTGCACTGTATGGACTGGGTTAAGAGAAAGAAAATGTCCTTAGTTAATAAAATCCTCAC

TGCTTTGGCAATCTCCAGAATTTTTCATCTCAGTTTATTGCTTATAAGTTTAGTCATATT
 CTTTTCATATTCTGATATTCCTATGACTTCAAGGATGACACAAGTCAGTAATAATGTTTG
 GATTATAGTCAATCATTTTCAGTATCTGGCTTTCTACATGCCTCAGTGTCTTTATTTTCT
 CAAGATATCCAATTTTCTAACTCTTTTTTTCTTTATCTAAAGTGGAGAGTTGAAAAAGT
 5 AGTTTCAGTTACACTGTTGGTGTGCTCCTCCTGATTTTAAATATTTTATTAATTAA
 CTTGGAAATTAGCATATGCATAAAGGAATGTCAAAGAAACATATCATGCAGCTTCAGTTC
 TCATTACTATGCAAAGTGTACAGGCAGGTGATAAGGCTTCACATTATTTTCCTGTCTGT
 CCCCGTTGTTTTGTCCCTGTCAACTTTTCTCCTGCTCATCTTCTCCCTGTGGACACTTCA
 CCAGAGGATGCAGCAGCATGTTTCAGGGAGGCAGAGATGCCAGAACCACGGCCCACTTCAA
 10 AGCCCTACAACTGTGATTGCATTTTTCTACTATATTCCATTTTTATTCTGTCTGTCTT
 AATACAAATATGAATTACTGAAGAAAATCTTTTCGTTGTATTTTGTGAGGTTGTATATA
 TAGCTTTTCCGACATTCCATTCATATATTCTGATTGTAGGAGACATGAAGCTGAGACAGG
 CCTGCCTGCCTCTCTGTATTATCGCAGCTGAAATTCAGACTACACTATGTAGAAATTTTA
 GATCACTAAAGTACTTTAGATTATGTTGTATATTCTAGACAAAAATTAAGTATACAAAT
 15 GTCTTTTGTATTTTTCATTTTAAATATCCTTTAATTTTGAAGTGCATGAAATTGATTTCTG
 CTTGCAATTATCACTGATTAAACTATTAATAATTTAACTAGTTGTATACAAGG

SEQ ID NO:107

20 Mouse T2R02 amino acid sequence

MESVLHNFATVLIYVEFIFGNLSNGFIVLSNFLDWVIKQKLSLIDKILLTLAISRITLIW
 EIYAWFKSLYDPSSFLIGIEFQIIYFSWVLSSHFSWLATTLSVFYLLRIANCSWQIFLY
 LKWRLKQLIVGMLLGSLVFLGNLMQSMLEERFYQYGRNTSVNTMSNDLAMWTELIFFNM
 25 AMFSVIPFTLALISFLLLI FSLWKHLQKMQLISRRHRDPSTKAHMNALRIMVSFLLLYTM
 HFLSLLISWIAQKHQSELADIIGMITELMYPVHSCILILGNSKLKQTS LCMLRHLRCRL
 KGENITIAYSNQITSFCVFCVANKSMR

30 **SEQ ID NO:108**

Mouse T2R02 nucleotide sequence

CAGCACAGTGAAAACTCATGGGCCACTTGGTCACCCAGGGACAGGCGACGCTGTTATAT
 GCCAAGCTTTCTATGAACATGGAATCTGTCCTTCACAACTTTGCCACTGTACTAATATAC

GTGGAGTTTATTTTTGGGAATTTGAGCAATGGATTCATAGTGTTGTCAAACCTTCTTGGAC
 TGGGTCATTAAACAAAAGCTTTCCTTAATAGATAAAATTCTTCTTACATTGGCAATTTCA
 AGAATCACTCTCATCTGGGAAATATATGCTTGGTTTAAAAGTTTATATGATCCATCTTCC
 TTTTAAATTGGAATAGAATTTCAAATTATTTATTTTAGCTGGGTCTTTCTAGTCACTTC
 5 AGCCTCTGGCTTGCCACAACTCTCAGCGTCTTTTATTTACTCAGAATAGCTAACTGCTCC
 TGGCAGATCTTTCTCTATTTGAAATGGAGACTTAAACAACTGATTGTGGGGATGTTGCTG
 GGAAGCTTGGTGTTCTTGCTTGGAAATCTGATGCAAAGCATGCTTGAAGAGAGGTCTAT
 CAATATGGAAGGAACACAAGTGTGAATACCATGAGCAATGACCTTGCAATGTGGACCGAG
 CTGATCTTTTTCAACATGGCTATGTTCTCTGTAATACCATTACATTGGCCTTGATTTCT
 10 TTTCTCCTGCTAATCTTCTCTTTGTGGAAACATCTCCAGAAGATGCAGCTCATTTCAGA
 AGACACAGAGACCCTAGCACCAAGGCCACATGAATGCCTTGAGAATTATGGTGTCTTC
 CTCTTGCTCTATACCATGCATTTCTGTCTCTTCTTATATCATGGATTGCTCAAAAGCAT
 CAGAGTGAAGTGGCTGATATTATTGGTATGATAACTGAACTCATGTATCCTTCAGTCCAT
 TCATGTATCCTGATTCTAGGAAATTCTAAATTAAAGCAGACTTCTCTTTGTATGCTGAGG
 15 CATTTGAGATGTAGGCTGAAAGGAGAGAATATCACAATTGCATATAGCAACCAAATAACT
 AGCTTTTGTGTATTCTGTGTTGCAAACAAATCTATGAGGTAGTTGTTCAAGGAATCCTTC
 CTTGACTTATTGTATCATGGAAGTCATATGGGGGAGTCTGAAAGAGCTGTCTTCTGTAAG
 CAAGGTTTGTATACACTAGTGGGGCTGGGACACCAACCCAAGCACAAAACCTAGCTATAA
 CCTATCCTGGCTGCAGGATATGCTGGAACAATGGTGGCTTGGAAATTGTGGGACTGGCAA
 20 AGCAATAGCTAGTCTAACTTGAGGCCCATTCACAGCAGGAAGCTCATGCCCACCTCTGC
 CTGGATGGCCAGGAAGCAAAATCTTGATGGCCCCAAGACCTATGGTAACTGAACACTAC
 TGGAAAAAGAAAGACTCGTGTTAATGATCTATCAAATATTTCTTAATGATATTCTGATAA
 ACTCATATATTAGTCCCTGTCCTAATCATCATCACTGGGACTCCTTCCCAGCACCTGATG
 GGAGCAGATAGAGATCTACATCCAAATAGTAAGTGTATCTTGGGGAACTCCACTTAAGAA
 25 TAGAAGGAACAATTATGAGAGCCAGAGTGATCCAGAACACTAGGATCACAGAATCAACTA
 AGCAGCATGCATAGGGGTAAATGGAGACTGAAGTGGCAATCACAGAGCCTGCATAGGTCT
 AACTAAGTCCTCTGTGTATATACTGTGGCTGTTTAGCTTAGGAATTTTGTGGACTCCT
 AACAAATGGATAAGGAATTC

30

SEQ ID NO:109

Mouse T2R03 amino acid sequence

MVLTIRAILWVTLITIIISLEFIIGILGNVFIALVNIIDWVKRGKISAVDKTYMALAISRT
AFLLSLITGFLVSLLDPALLMRTMVRLLTISWMVTNHFSVWFATCLSIIFYFLKIANFSN
SIFLVLKWEAKKVSVTLVVSVIIILIMNIIIVINKFTDRLQVNTLQNCSTSNLTKDYGLFL
FISTGFTLTPFAVSLTMFLLLIIFSLWRHLKNMCHSATGSRDVSTVAHIKGLQTVVTFLLL
5 YTAFVMSLLSESLNINIQHTNLLSHFLRSIGVAFPTGHSCVLILGNSKLRQASLSVILWL
RYKYKHIEHWGP

SEQ ID NO:110

10 Mouse T2R03 nucleotide sequence

CTTTAATAGCAGGGTGTGAATATTTAAATTTTCTTCTGCAGCAACTACTGAGGGCTTCA
GACTGCTGTATACAGGGCATGAAGCATCTGGATGAAGTTCAGCTGTGCTGCCTTTGACAA
CAATTTTTTGTGTATGTGTGGAGAACATAAACCATTTCATTAGTGAAATTTGGCTTTTGG
15 GTGACATTGTCTATGATAGTTCTGAAAGTGATTATGTTAAGAATCAGACACAGCCGTCTA
GAAGATTGTATTAACACATCTTTGGTAGTTCAGAAGAAATTAGATCATC**ATGGTGTTGAC**
AATAAGGGCTATTTTATGGGTAACATTGATAACTATTATAAGTCTGGAGTTTATCATAGG
AATTTTAGGAAATGTATTCATAGCTCTCGTGAACATCATAGACTGGGTAAAGAGGAAA
GATCTCTGCAGTGGATAAGACCTATATGGCCCTGGCCATCTCCAGGACTGCTTTTTTATT
20 **GTCACTAATCACAGGGTTCTTGGTATCATTATTGGACCCAGCTTTATTGGGAATGAGAAC**
GATGGTAAGGCTCCTTACTATTTCTCGATGGTGACCAATCATTTAGTGTCTGGTTTGC
AACATGCCTCAGTATCTTTTATTTTCTCAAGATAGCTAATTTCTCAAATTCTATTTTCCT
TGTTCTCAAATGGGAAGCTAAAAAGTGGTATCAGTGACATTGGTGGTATCTGTGATAAT
CTTGATCATGAACATTATAGTCATAACAAATTCAGTGACAGACTTCAAGTAAACACACT
25 **CCAGAACTGTAGTACAAGTAACACTTTAAAGATTATGGGCTCTTTTTATTATTAGCAC**
TGGGTTTACACTCACCCCATTCGCTGTGTCTTTGACAATGTTTCTTCTGCTCATCTTCTC
CCTGTGGAGACATCTGAAGAATATGTGTCACAGTGCCACAGGCTCCAGAGATGTCAGCAC
AGTGGCCACATAAAAGGCTTGCAAAGTGTGGTAACCTTCCTGTTACTATATACTGCTTT
TGTTATGTCACCTTCTTTCAGAGTCTTTGAATATTAACATTCAACATACAAATCTTCTTTC
30 **TCATTTTTTACGGAGTATAGGAGTAGCTTTTCCACAGGCCACTCCTGTGTACTGATTCT**
TGGAAACAGTAAGCTGAGGCAAGCCTCTCTTCTGTGATATTGTGGCTGAGGTATAAGTA
CAAACATATAGAGAATTGGGGCCCCTAAATCATATCAGGGATCCTTTTCCACATTCTAGA
AAAAAATCAGTTAATAAGAACAGGAATTTAGGAAGGAATCTGAAATTATGAATCTCATAG
GCCATGAACCTTCAGACAAAGGATTATTAGAGAGATAGAGAGAGAACATTGTTATCTGT

AACTCGACAGGCAACACTGTAGATTATGAAAATAAATGTCAGTCTGTAATGGAAAGCAA
ACATGCTATATTTTATTAATTGGTTTTGGTTTAAGGTCGGGATA

5 **SEQ ID NO:111**

Mouse T2R04 amino acid sequence

MLSALESILLSVATSEAMLGVLGNTFIVLVNYTDWVRNKKLSKINFILTGLAISRIFTIW
IITLDAYTKVFLLTMLMPSSLHECMSYIWVIINHLSVWFSTSLGIFYFLKIANFSHYIFL
10 WMKRRADKVFVFLIVFLIITWLASFPLAVKVIKDVKIYQSNTSWLIHLEKSELLINYVFA
NMGPISLFIVAI IACFLLTISLWRHSRQMOSIGSGFRDLNTEAHMKAMKVLIAFIILFIL
YFLGIL IETLCLFLTNNKLLFIFGFTLSAMYPCCHSFILILTSRELKQDTMRALQRLKCC
ET

15

SEQ ID NO:112

Mouse T2R04 nucleotide sequence

CTGCAGCAGGTAAATCACACCAGATCCAGCAGAAGCCTTCTTGGAATTGGCAGAGATGC
20 TGAGTGCACTGGAAAGCATCCTCCTTTCTGTTGCCACTAGTGAAGCCATGCTGGGAGTTT
TAGGGAACACATTTATTGTACTTGTAACACTACACAGACTGGGTCAGGAATAAGAACTCT
CTAAGATTAACTTTATTCTCACTGGCTTAGCAATTTCCAGGATTTTTACCATATGGATAA
TAACTTTAGATGCATATACAAAGGTTTTCTTCTGACTATGCTTATGCCGAGCAGTCTAC
ATGAATGCATGAGTTACATATGGGTAATTATTAACCATCTGAGCGTTTGGTTTAGACCA
25 GCCTCGGCATCTTTTATTTTCTGAAGATAGCAAATTTTCCCACTACATATTTCTCTGGA
TGAAGAGAAGAGCTGATAAAGTTTTTGTCTTTCTAATTGTATTCTTAATTATAACGTGGC
TAGCTTCCTTTCCGCTAGCTGTGAAGGTCATTAAAGATGTTAAATATATCAGAGCAACA
CATCCTGGCTGATCCACCTGGAGAAGAGTGAGTTACTTATAAACTATGTTTTTGCCAATA
TGGGGCCCATTTCCCTCTTTATTGTAGCCATAATTGCTTGTTTCTTGTTAACCATTTCCC
30 TTTGGAGACACAGCAGGCAGATGCAATCCATTGGATCAGGATTCAGAGATCTCAACACAG
AAGCTCACATGAAAGCCATGAAAGTTTTAATTGCATTTATCATCCTCTTTATCTTATATT
TTTTGGGTATTCTCATAGAAACATTATGCTTGTTTCTTACAAACAATAAACTTCTCTTTA
TTTTTGGCTTCACTTTGTCAGCCATGTATCCCTGTTGCCATTCTTTATCCTAATTCTAA
CAAGCAGGGAGCTGAAGCAAGACACTATGAGGGCACTGCAGAGATTAAAATGCTGTGAGA

CTTGACAGAGAAATGAATGTTCTGGCACAGTTCAGCAGGGAATCCCTGGAGCCCTTTCCA
TTCCCACATATGTTCTCACACTGTCTTTAGTTGAATTGTTAAAAGTTTTTGAAACCTTTGG
CAACTGATTGACTGCAGCTACGCCAGTGTAAGATTTTCATAGTAAGAGCAAACATTGAAA
ATAAGACTTCTCAGTCTTATTTCAATTGAGTTTCTAAAGCATTGACACCCATTCACCAGAA
5 AAACCAAAGGGGAAGAGAGGAGTTTTTCAGACATGTGTGATGAATCTTGATATTTAGGACA
TGGAATTGAGGAG~CCAGAGGGATGCTACCGTGTGTCTACAGCTTTGTTTGTTAAATAGC
TACTTTTCCTTTCCAGTTAGTTAAAGTAGATGCTTGGAGTAGTGGTGAAAATCATGGCA
GTAGATGGGATCTGTGGGAAGTGGTTGAGGAAGCAGGCTGTTTCTGAACGAAGAGACCAG
AGGACTGATTGAACTGGTCATTGTGTATATCAAAAATAGTGATTTTCAGATGAAGCCAAGT
10 TGTAGAGCAAAGATATCTGAGGAAGAATTC

SEQ ID NO:113

Mouse T2R05 amino acid sequence

15 MLSAAEGILLSIATVEAGLGVLGNTFIALVNCMDWAKNNKLSMT**T**GFLLI GLATSRI FIVW
LLTLDAYAKLFYPSKYFSSSLIEI**I**SYIWMTVNHLTVWFATSLSIFYFLKIANFSDCVFL
WLKRRTDKAFVFLLGCLL**T**SWVISFSFVVKVMKD**G**KVNHRNRTSEMYWEKRQFTINYVFL
NIGVISL FMMTLTACFL LMSLWRHSRQM QSGVSGFRDLNTEAHVKA IKFLISFIILFVL
20 YFIGVSIEI**I**CIFIPENKLLFIFGFTTASIYPCCHSFILILSNSQLKQAFVKV**L**QGLKFF

SEQ ID NO:114

Mouse T2R05 nucleotide sequence

25 **ATGCTGAGTGCGGCAGAAGGCATCCTCCTTTCCATTGCAACTGTTGAAGCTGGGCTGGGA**
GTTTTAGGGAACACATTTATTGCACTGGTAAACTGCATGGACTGGGCCAAGAACAATAAG
CTTCTATGACTGGCTTCCTTCTCATCGGCTTAGCAACTTCAGGATTTTTATTGTGTGG
CTATTAACTTTAGATGCATATGCAAAGCTATTCTATCCAAGTAAGTATTTTTCTAGTAGT
30 **CTGATTGAAATCATCTCTTATATATGGATGACTGTGAATCACCTGACTGTCTGGTTTGCC**
ACCAGCCTAAGCATCTTCTATTTCTGAAGATAGCCAATTTTTCCGACTGTGTATTTCTC
TGGTTGAAGAGGAGAACTGATAAAGCTTTTGTTTTTCTCTTGGGGTGTTTGCTAACTTCA
TGGGTAATCTCCTTCTCATTTGTTGTGAAGGTGATGAAGGACGGTAAAGTGAATCATAGA
AACAGGACCTCGGAGATGTACTGGGAGAAAAGGCAATTCACTATTAACCTACGTTTTCTC

AATATTGGAGTCATTTCTCTCTTTATGATGACCTTAACCTGCATGTTTCTTGTTAATTATG
TCACCTTGGAGACACAGCAGGCAGATGCAGTCTGGTGTTTCAGGATTCAGAGACCTCAAC
ACAGAAGCTCATGTGAAAGCCATAAAATTTTAAATTCATTTATCATCCTTTTCGTCTTG
TATTTTATAGGTGTTTCAATAGAAATTATCTGCATATTTATAACCAGAAAACAACTGCTA
5 TTTATTTTTGGTTTCACAACTGCATCCATATATCCTTGCTGTCACTCATTTATTCTAATT
CTATCTAACAGCCAGCTAAAGCAAGCCTTTGTAAAGGTACTGCAAGGATTAAAGTTCTTT
TAG

10 **SEQ ID NO:115**

Mouse T2R06 amino acid sequence

MLTVAEGILLCFVTSGSVLGLGNGFILHANYINCVRKKFSTAGFILTGLAICRIFVICI
IISDGYLKLFSPhMVASDAHIIVISYIWVIINHTSIWFATSLNLFYLLKIANFSHYIFFC
15 LKRRINTVFIFLLGCLFISWSIAFPQTVKIFNVKKQHRNVSWQVYLYKNEFIVSHILLNL
GVIFFFMVAIITCFLLIISLWKHNRMQLYASRFKSLNTEVHVKVMKVLISFIILLILHF
IGILIIETLSFLKYENKLLLLILGLIISCMYPCCHSFILILANSQKQASLKALKQLKCHKK
DKDVRVTW

20

SEQ ID NO:116

Mouse T2R06 nucleotide sequence

TATAGTTGCAGCAGAAGCAACGTTAGGGATCTGTAGAGATGCTGACTGTAGCAGAAGGAA
25 TCCTCCTTTGTTTTGTAAGTAGTGGTTCAGTCCTGGGAGTTCTAGGAAATGGATTTATCC
TGCATGCAAACTACATTAACCTGTGTCAGAAAGAAGTTCTCCACAGCTGGCTTTATTCTCA
CAGGCTTGGCTATTTGCAGAATCTTTGTCATATGTATAATAATCTCTGATGGATATTTAA
AATTGTTTTCTCCACATATGGTTGCCTCTGATGCCACATTATAGTGATTTCTTACATAT
GGGTAATTATCAATCATAACAAGTATATGGTTTGCCACCAGCCTCAACCTCTTCTATCTCC
30 TGAAGATAGCAAATTTTTCTCACTACATCTTCTTCTGCTTGAAGAGAAGAATCAATACAG
TATTTATCTTTCTCCTGGGATGCTTATTTATATCATGGTCAATTGCTTTCCACAAACAG
TGAAGATATTTAATGTTAAAAGCAGCACAGAAATGTTTCCTGGCAGGTTTACCTCTATA
AGAATGAGTTCATtGTAAGCCACATTCTTCTCAACCTGGGAGTTATATTCTTCTTTATGG
TGGCTATCATTACATGCTTCCTATTAATTATTTCACTTTGGAAACATAACAGAAAGATGC

AGTTGTATGCCTCAAGATTCAAAGCCTTAACACAGAAGTACATGTGAAAGTCATGAAAG
 TTTTAATTTCTTTTATTATCCTGTTAATCTTGCATTTTCATAGGGATTTTGATAGAAACAT
 TGAGCTTTTTTAAAATATGAAAATAAACTGCTACTTATTTTGGGTTTGATAATTCATGCA
 TGTATCCTTGCTGTCATTCATTTATCCTAATTCTAGCAAACAGTCAGCTGAAGCAGGCTT
 5 CTTTGAAGGCACTGAAGCAATTAAAATGCCATAAGAAAGACAAGGACGTCAgAGTGACAT
 GGTAGACTTATGGAGAAATGAATGGTCACAAGAAATAGCCTGGTGTGGAGATGTTGATAT
 CTCTAAAGACCGTTTCACTTCCAAATTCTTGCAATTATTTAAAAAAAAGTCTTGCTGA
 TATCATGGAATCATGGGAAATGTTGCAATTGTGTTTTGGGGACAGGGTGACCAGTGAAGG
 TATGGTTAAGCAGCGAAACACTCATAACAGCTCGTTTCGTTCTTTTTGTATTTTATTTTGTG
 10 TTGGTGGCCTTCCAAGACATGATTTCTCTATGTAAGTTTTTG

SEQ ID NO:117

Mouse T2R07 amino acid sequence

15 MLNSAEGILLCVVTSEAVLGVLGDTYIALFNCMDYAKNKKLSKIGFILIGLAISRIGVW
 I I I L Q G Y I Q V F F P H M L T S G N I T E Y I T Y I W V F L N H L S V W F V T N L N I L Y F L K I A N F S N S V F L
 W L K R R V N A V F I F L S G C L L T S W L L C F P Q M K I L Q N S K M H Q R N T S W V H Q R K N Y F L I N Q S V T N
 L G I F F F I I V S L I T C F L L I V F L W R H V R Q M H S D V S G F R D H S T K V H V K A M K F L I S F M V F F I L H
 20 F V G L S I E V L C F I L P Q N K L L F I T G L T A T C L Y P C G H S I I V I L G N K Q L K Q A S L K A L Q Q L K C C E
 T K G N F R V K

SEQ ID NO:118

25 Mouse T2R07 nucleotide sequence

TTCATAATGAAGAGGAGGCAGGGCAATGTTGGTTTTCTGTTGTCTGACCAGTGTATTTGAC
 AGTGATACTACACATTTGATTGCTAAATGCAAATAGTTCCAAAGGAACAAGTAAATTTTA
 TGAAATAGAAGCTTCTATTTGCTTATTAACAAACTGCAAGCAAACATTAGTCTGCACACA
 30 TTTTATAGACAAGCTAAATCTTCAAAGCAATAAAAAAGAGCACCCATAAAGTTCTGACT
 CTATCACATGACAATAGGCTTGAAAAGATTGTCTATGTAGATAAAGAAGATGGCATAACT
 TCTCCATCAAGAAGCCAGTATATGGGACATTCTCCAGCAGATAATTTACAATAGATGCAG
 CAGAAGTAACCTTAGAGATCTGTAAAGATGCTGAATTCAGCAGAAGGCATCCTCCTTTGT
 GTTGTCACTAGTGAGGCTGTGCTCGGAGTTTTAGGGGACACATATATTGCACTTTTTTAAC

TGCATGGACTATGCTAAGAACAAGAAGCTCTCTAAGATCGGTTTCATTCTCATTGGCTTG
 GCGATTTCCAGAATTGGTGTGTATGGATAATAATTTTACAAGGGTATATACAAGTATTT
 TTTCCACACATGCTTACCTCTGGAAACATAACTGAATATATTACTTACATATGGGTATTT
 CTCAATCACTTAAGTGTCTGGTTTGTACCAACCTCAACATCCTCTACTTTCTAAAGATA
 5 GCTAATTTTTCCAACCTCTGTATTTCTCTGGCTGAAAAGGAGAGTCAATGCAGTTTTTATC
 TTTCTGTCAGGATGCTTACTTACCTCATGGTTACTATGTTTTCCACAAATGACAAAGATA
 CTTCAAAATAGTAAAATGCACCAGAGAAACACATCTTGGGTCCACCAGCGGAAAAATTAC
 TTTCTTATTAACCAAAGTGTGACCAATCTGGGAATCTTTTTCTTCATTATTGTATCCCTG
 ATTACCTGCTTTCTGTTGATTGTTTTCTCTGGAGACATGTCAGACAAATGCACTCAGAT
 10 GTTTCAGGATTCAGAGACCACAGCACAAAAGTACATGTGAAAGCTATGAAATTTCTAATA
 TCTTTTATGGTCTTCTTTATTCTGCATTTTGTAGGCCTTTCCATAGAAGTGCTATGCTTT
 ATTCTGCCACAAAATAAACTGCTCTTTATAACTGGTTTGACAGCCACATGCCTCTATCCC
 TGCGGTCACTCAATCATCGTAATTTTAGGAAATAAGCAGTTAAAGCAAGCCTCTTTGAAG
 GCACTGCAGCAACTAAAATGCTGTGAGACAAAAGGAAATTTTCAGAGTCAAATAAATGGGT
 15 TTGCAAATAAATAGCTGCCTTGTTCTTCACTGGTTTTTACCCTGTTAGTTGATGTTATG
 AAAAGTTCCTGCTATGGTTGATGACATCTCAAGGAATCTATTTTTCTGGTGGCATGTTAA
 GTCCACGTGAAGCCTCACTTCATACTGTGACTTGACTATGCAAATTCTTTCCACAAAATA
 ACCAGATAACATTCAGCCTGGAGATAAATTCATTTAAAGGCTTTTATGGTGAGGATAAAC
 AAAAAAAAAAATCATTTTTCTGTGATTCCTGTAACCTCCCAGGATGAGTAAAGAAAAC
 20 AAGACAAATGGTTGTGATCAGCCTTTGTGTGTCTAGACAGAGCTAGGGACCAGATGTTGA
 TGCTTGTGTGTGGTTTTGAGTTCTTTAAGAAGTTATTGCCTCTCTGCCATTTCGGTATTCC
 TCAGGTGAGAATTC

25 **SEQ ID NO:119**

Mouse T2R08 amino acid sequence

MLWELYVFVFAASVFLNFVGIIANLFIIIVIIIKTWVNSRRIASPDRILFSLAITRFLTGL
 LFLSNSVYIATNTGRSVYFSTFFLLCWKFLDANSLWLVTILNSLYCVKITNFQHPVFLLL
 30 KRTISMKTTSLLLACLLISALTLLYYMLSQISRFP EHIIGRNDTSFDLSDGILTLVASL
 VLNSLLQFMLNVTFASLLIHSLRRHIQKMQRNRTSFWNPQTEAHMGAMRLMICFLVLYIP
 YSIATLLYLPSYMRKNLRAQAICMIITAAYPPGHSVLLIITHHKLKAKAKKIFCFYK

SEQ ID NO:120

Mouse T2R08 nucleotide sequence

AAGCTTGTTTGTAAATTAGGCATTCCTAAGAAAATAAGAACAGGAGTGAAGAAATAGTAAT
5 TTAATCCTTGAAAGATTTGCATCTCAGTAAAAGCAGCTGCCTCTTAGACCAGAAATGGTG
TTTGCCATGCTGGAAAATAAAAAGGAGACCTCTTTCCAGGCTGCATCCTGTGTCTGCTTA
CTTATTTTCAGTTTGTTTTTCATCGGCACCAAACGAGGAAAG**ATGCTCTGGGAACTGTATGT**
ATTTGTGTTTGCTGCCTCGGTTTTTTTTTAAATTTTGTAGGAATCATTGCAAATCTATTTAT
TATAGTGATAATTATTAAGACTTGGGTCAACAGTCGCAGAATTGCCTCTCCGGATAGGAT
10 **CCTGTTTCAGCTTGGCCATCACTAGATTCCTGACTTTGGGGTTGTTTCTACTGAACAGTGT**
CTACATTGCTACAAATACTGGAAGGTCAGTCTACTTTTCCACATTTTTTCTATTGTGTTG
GAAGTTTCTGGATGCAAACAGTCTCTGGTTAGTGACCATTCTGAACAGCTTGTATTGTGT
GAAGATTACTAATTTTCAACACCCAGTGTTTCTCCTGTTGAAACGGACTATCTCTATGAA
GACCACCAGCCTGCTGTTGGCCTGTCTTCTGATTTTCAGCCCTCACCCTCTCCTATATTA
15 **TATGCTCTCACAGATATCACGTTTTCTGAACACATAATTGGGAGAAATGACACGTCATT**
TGACCTCAGTGATGGTATCTTGACGTTAGTAGCCTCTTTGGTCCTGAACTCACTTCTACA
GTTTATGCTCAATGTGACTTTTGCTTCCTTGTTAATACATTCCTTGAGAAGACATATACA
GAAGATGCAGAGAAACAGGACCAGCTTTTGGAAATCCCAGACGGAGGCTCACATGGGTGC
TATGAGGCTGATGATCTGTTTCCTCGTGCTCTACATTCATATTCAATTGCTACCCTGCT
20 **CTATCTTCCTTCCTATATGAGGAAGAATCTGAGAGCCCAGGCCATTTGCATGATTATTAC**
TGCTGCTTACCCTCCAGGACATTCTGTCTCCTCATTATCACACATCATAACTGAAAGC
TAAAGCAAAGAAGATTTTCTGTTTCTACAAGTAGCAGAATTCATTAGTAGTTAACAGCA
TCAATTCATGGTTTGGTTGCATTAGAAATGTCTCAGTGATCTAAGGACTTAATTTTGTGA
TCTTGATCTGGCATCCTGACCCTGAGACTAAGTGCTTATATTTTGGTCAATACAGCATC
25 **TTTTGGCTAATATTTTAAAGTAAATCACATTCCATAAGAAATTGTTTAAGGGATTACGT**
ATTTTTTCATGGCTATCACATTCCTAGACAATGGAAATCACCATACTGTTTCGCTAGCTAC
TGAAGTACCAGGGGAAAGTCCATGAATGAAGGCCACATTGTGATGTTCTTGGTTAGCACA
GATTAGAGAATTTGGCCTCAACTGAGCAAGATATC

30

SEQ ID NO:121

Mouse T2R09 amino acid sequence

MEHLLKRTFDITENILLIILFIELIIGLIGNGFTALVHCMDWVKRKKMSLVNKILTALAT
SRIFLLWFMLVGFPISSLYPYLVTTRLMIQFTSTLWTIANHISVWFATCLSVFYFLKIAN
FSNSPFLYLKRRVEKVSVTLLVSLVLLFLNILLNLEINMCINEYHQINISYIFISYYH
LSCQIQVLGSHIIFLSVPVVLSTFLLLI FSLWTLHKRMQQHVQGGRDARTTAHFALQ
5 AVIAFLLLYSIFILSLLQFWIHGLRKKPPFIAFCQVVDTAFFPSFHSYVLILRDRKLRHA
SLSVLSWLKCRPNYVK

SEQ ID NO:122

10 Mouse T2R09 nucleotide sequence

GAATTCAGAAATCATCAAAAAATCTTCAAACTACATGTTTAAAATAGCACTTCAAATGA
ATACATTTGCAAATCTTTACAATAACATAAAAATGGAGCATCTTTTGAAGAGAACATT
TGATATCACCGAGAACATACTTCTAATTATTTTATTCATTGAATTAATAATTGGACTTAT
15 **AGGAAACGGATTCACAGCCTTGGTGCACTGCATGGACTGGGTAAAGAGAAAAAAATGTC**
ATTAGTTAATAAAATCCTCACCGCTTTGGCAACTTCTAGAATTTTCCTGCTCTGGTTCAT
GCTAGTAGGTTTTCCAATTAGCTCACTGTACCCATATTTAGTTACTACTAGACTGATGAT
ACAGTTCACTAGTACTCTATGGACTATAGCTAACCATATTAGTGTCTGGTTTGCTACATG
CCTCAGTGTCTTTTATTTTCTCAAGATAGCCAATTTTCTAATTCTCCTTTTCTCTATCT
20 **AAAGAGGAGAGTTGAAAAGTAGTTTCAGTTACATTACTGGTGTCTCTGGTCCTCTTGTT**
TTTAAATATTTTACTACTTAATTTGGAAATTAACATGTGTATAAATGAATATCATCAAT
AAACATATCATACATCTTCATTTCTTATTACCATTTAAGTTGTCAAATTCAGGTGTTAGG
AAGTCACATTATTTTCCTGTCTGTCCCCGTTGTTTTGTCCCTGTCAACTTTTCTCCTGCT
CATCTTCTCCCTGTGGACACTTCACAAGAGGATGCAGCAGCATGTTCAAGGAGGCAGAGA
25 **TGCCAGAACCACGGCCCACTTCAAAGCCTTGCAAGCAGTGATTGCCTTTCTCCTACTATA**
CTCCATTTTTATCCTGTCACTGTTACTACAATTTTGGATCCATGGATTAAGGAAGAAACC
TCCTTTCATTGCATTTTGTGAGGTGTAGATACAGCTTTTCCTTCATTCCATTCATATGT
CTTGATTCTGAGAGACAGGAAGCTGAGACACGCCTCTCTCTGTGTTGTCGTGGCTGAA
ATGCAGGCCAAATTATGTGAAATAATATTTCTTTGTATTTTCATTTTCAATTTTAAAATA
30 **TTCTTAGAATTTGACTGCATGTATTTTCATCTTTTATTTGAAACAACCACTAATTAAAGCT**
ATTACTAATTTAGCAAGTCGTATACAAGGTTATTTTTTAATACACATATCAAAAACCTGAC
ATGTTTATGTTCTACAAAAACCTGAATATATCAAAATTATATAAATTTTGTATCAACGAT
TAACAATGGAGTTTTTTTTATTTATGACCTGTCACGGGACTCCGGTGGAGTCAGCTTGTC
GATGAAAGTCTGAAAGCTT

SEQ ID NO:123

Mouse T2R10 amino acid sequence

5
MFSQIISTSDIFTFTIILFVELVIGILGNGFIALVNIMDWTKRRSISSADQILTALAITR
FLYVWFMIICILLFMLCPHLLTRSEIVTSIGIIWIVNNHFSVWLATCLGVFYFLKIANFS
NSLFLYLKWRVKKVVLMI IQVSMIFLIILNLLSLSMYDQFSIDVYEGNTSYNLGDSTPFPT
ISLFINSSKVFVITNSSHIFLPINSLFMLIPFTVSLVAFMLLIFSLWKHHKMQVNAKPP
10 RDASTMAHIKALQTGFSLLLYAVYLLFIVIGMLSLRLIGGKLILLFDHISGIGFPISHS
FVLILGNNKLRQASLSVLHCLRCRSKDMDTMGP

SEQ ID NO:124

15 Mouse T2R10 nucleotide sequence

GAATTCAACATCTTATTCAACTTCAGAAAACCTGGATATTAGACACAGTGTCTGGATGAAG
CAGAGGTGATCTCTTTGGGAAAAAAGCCAAGTAGTCATAAAGAATTTATGAAACAATTC
CTGGGATTGTTTATATTTGTTACAAACAAATTTATATGTTTGTAGTCAGTAATGTATAA
20 GTGGGATTTTAAAGCATGATTATCTTGAATTTTAAACAAAAACATGTAGTGCTTTTTAA
ATGTAGCAGAAACATTAAAAATTGAAGCATGTTCTCACAGATAATAAGCACCAGTGATAT
TTTTACTTTTACAATAATATTATTTGTGGAATTAGTAATAGGAATTTTAGGAAATGGATT
CATAGCACTAGTGAATATCATGGACTGGACCAAGAGAAGAAGCATTTCATCAGCGGATCA
GATTCTCACTGCTTTGGCCATTACCAGATTTCTCTATGTGTGGTTTATGATCATTTGTAT
25 ATTGTTATTCATGCTGTGCCACATTTGCTTACAAGATCAGAAATAGTAACATCAATTGG
TATTATTTGGATAGTGAATAACCATTTTCAGCGTTTGGCTTGCCACATGCCTCGGTGTCTT
TTATTTTCTGAAGATAGCCAATTTTCTAACTCTTTGTTTCTTTACCTAAAGTGGAGAGT
TAAAAAGTAGTTTTAATGATAATACAGGTATCAATGATTTTCTTGATTTTAAACCTGTT
ATCTCTAAGCATGTATGATCAGTTCTCAATTGATGTTTATGAAGGAAATACATCTTATAA
30 TTTAGGGGATTCAACCCCATTTCCACAAATTTCTTATTCATCAATTCATCAAAGTTTT
CGTAATCACCAACTCATCCCATATTTTCTTACCCATCAACTCCCTGTTTCATGCTCATACC
CTTCACAGTGTCCCTGGTAGCCTTTCTCATGCTCATCTTCTCACTGTGGAAGCATCACAA
AAAGATGCAGGTCAATGCCAAACCACCTAGAGATGCCAGCACCATGGCCACATTAAAGC
CTTGCAAACAGGGTTCTCCTTCCTGCTGCTGTATGCAGTATACTTACTTTTTATTGTCAT

AGGAATGTTGAGCCTTAGGTTGATAGGAGGAAAATTAATACTTTTATTTGACCACATTTCTGGAATAGGTTTTCTATAAGCCACTCATTTGTGCTGATTCTGGGAAATAACAAGCTGAGACAAGCCAGTCTTTCAGTGTTGCATTGTCTGAGGTGCCGATCCAAAGATATGGACACCATGGGTCCATAAAAAATTTAGAGGTCATTGGGAAACATTTTGAGATCTTATAGGGGAAAAA
5 GAAAATGTGGGGCTTCAAAGCTGGTAGGAGTAATATAGAGAAGGATAGGAG

SEQ ID NO:125

Mouse T2R11 amino acid sequence

10

MEHPLRRTFDFSQSILLTILFIELIIGLIRNGLMVLVHCIDWVKRKKFHLLIKSSPLWQTSRICLLWFMLIHLLITLLYADLASTRTMMQFASNPTISNHISIWLATCLGVFYFLKIANFSNSTFLYLKWRVQFLLLNILLVKFEINMWINEYHQINIPYSFISYYQXCQIQVLSLHII
15 FLSVPFILSLSTFLLLIIFSLWTLHQRMQQHVQGYRDASTMAHFKALQAVIAFLLIHSIFI
LSLLLQLWKHELRRKKPPFVFCQVAYIAFPSSHSYVFILGDRKLRQACLSVLWRLKCRPN
YVG

SEQ ID NO:126

20 Mouse T2R11 nucleotide sequence

AATAATGTATGTGGAAGAGTTAAGTATAAATGTTGTATGAGAATGAACTCAGAAATCATCAAAAATCTTTAAACTGCATGTTAAAAATCACACTTCAAATGAATATATTTGTAATTCTTTAGAACTAATAAATAAAATGGAGCATCCTTTGAGGAGAACATTTGATTTCTCCCAGAGCA
25 TACTTCTAACCATTTTATTCATTGAATTAATAATTGGACTTATAAGAAATGGATTAATGG
TATTGGTGCCTGCATAGATTGGGTAAAGAGAAAAAATTCATTTGTTAATCAAATCCT
CACCCTTTGGCAAACCTTCCAGAATTTGTCTGCTCTGGTTCATGCTAATACATCTCCTGATTACTTTATTGTATGCAGATTTAGCTAGTACTAGAACGATGATGCAATTCGCTAGCAATCATGGACTATATCTAACCATATCAGCATCTGGCTTGCTACATGCCTTGGTGTCTTTTATT
30 TTCTCAAGATAGCCAATTTTCTAACTCTACTTTTCTCTATCTAAAATGGCGAGTTCAGT
TCCTCTTGTTAAATATTTTACTGGTTAAATTTGAGATTAACATGTGGATAAATGAATATCATCAAATAAACATACCATACAGCTTCATTTCTTATTACCAAATTGTCAAATACAGGTGTT
AAGTCTTCACATTATTTTCCTGTCTGTCCCCTTTATTTTGTCCCTGTCAACTTTTCTCCT
GCTCATCTTCTCCCTGTGGACACTTCACCAGAGGATGCAGCAGCATGTTCAAGGATACAG

AGATGCCAGCACAAATGGCCCACTTCAAAGCCTTGCAAGCAGTGATTGCCTTTCTCTTAAT
ACACTCCATTTTTATCCTGTCAGTGTACTACAACCTTTGGAAACATGAATTAAGGAAGAA
ACCTCCTTTTGTGTATTTTGTGTCAGGTTGCATATATAGCTTTTCCTTCATCCCATTCTATA
TGTCTTCATTCTGGGAGACAGAAAGCTGAGACAGGCTTGTCTCTCTGTGTTGTGGAGGCT
5 GAAATGCAGGCCAAATTATGTGGGATAAAATCTCTTTGTGCTTTCATTTCCAATTCTTAA
ATATTCTTTGATTTTGACTGCATAAATT

SEQ ID NO:127

10 Mouse T2R12 amino acid sequence

GAIVNVDFLIGNVGNFIVVANIMDLVKRRKLSSVDQLLTALAVSRITLLWYLYIMKRTF
LVDPNIGAIMQSTRLTNVIWIIISNHFSIWLATTLSTIFYFLKIANFSNSIFCYLRWRFEKV
ILMALLVSLVLLFIDILVTNMYINIWTDEF

15

SEQ ID NO:128

Mouse T2R12 nucleotide sequence

20 TTTTCAGCAGTGACTTTGGGAAGCAGAACGTCCTCTTAGAGACAGTGGGTGCTGCTATCC
TAGTTAATGTGGAGCAATAGTTAATGTGGATTTCTAATTGGAAATGTTGGGAATGGATT
CATTGTTGTGGCAAACATAATGGACTTGGTCAAGAGAAGAAAGCTTCTTCAGTGGATCA
GCTGCTCACTGCACTGGCCGTCTCCAGAATCACTTTGCTGTGGTACCTGTACATAATGAA
ACGAACATTTTTAGTGGATCCAAACATTGGTGCAATTATGCAATCAACAAGACTGACTAA
25 TGTTATCTGGATAATTTCTAACCATTTTAGTATATGGCTGGCCACCACCCTCAGCATCTT
TTATTTTCTCAAGATAGCAAATTTTCTAACTCTATTTTCTGTTACCTGAGGTGGAGATT
TGAAAAGGTGATTTTGATGGCATTGCTGGTGTCCCTGGTCCTCTTGTTTATAGATATTTT
AGTAACAAACATGTACATTAATATTTGGACTGATGAATTC

30

SEQ ID NO:129

Mouse T2R13 amino acid sequence

MVAVLQSTLPPIIFSMEFIMGTLGNGFIFLIVCIDWVQRRKISLVDQIRTALAISRIALIW
LIFLDWWVSVHYPALHETGKMLSTYLISWTVINHCNFWLTANLSILYFLKIANFSNII FL
YLKFRSKNVVLVTLVSLFFLFLNTV I I K I FSDVCFDSVQRNVSQIFIMYNHEQICKFLS
FTNPMFTFIPFVMSTVMFSLLI FSLWRHLKNMQHTAKGCRDISTTVHIRALQTIIVSVVL
5 YTIFFLSFFVKVWSFVSPERYLI FLFVWALGNAVFSAHPFVMILVNRRLRLASLSLI FWL
WYRFKNIEV

SEQ ID NO:130

10 Mouse T2R13 nucleotide sequence

AAGCTTGTGTTTGGATGAATTCTATTTATGTCTATCAATTTAAGATTTTCATATGA
ATCATTAAAGAAATCTTGATAGTTGTTTGTGAGATATCACTTCTGCAATTTTAAATGAAA
TTACACTCATATTTTGAAGGAACAATATGTTTTAAAGGAATATATTAACAAATCTTCAGC
15 AGTTACCTCAGAAGTTTGGGTATTGTTTTACAGAAAATGGTGGCAGTTCTACAGAGCACA
CTTCCAATAATTTTCAGTATGGAATTCATAATGGGAACCTTAGGAAATGGATTCAATTTT
CTGATAGTCTGCATAGACTGGGTCCAAAGAAGAAAAATCTCTTTAGTGGATCAAATCCGC
ACTGCTCTGGCAATTAGCAGAATCGCTCTAATTTGGTTGATATTCCTAGATTGGTGGGTG
TCTGTTCAATTACCCAGCATTACATGAACTGGTAAGATGTTATCAACATATTTGATTTCC
20 TGGACGGTGATCAATCATTGTAACTTTTGGCTTACTGCAAACTTGAGCATCCTTTATTTT
CTCAAGATAGCCAACTTTTCTAACATTATTTTTCTTTATCTAAAGTTTAGATCTAAAAAT
GTGGTATTAGTGACCCTGTTAGTGTCTCTATTTTTCTTGTTCTTAAATACTGTAATTATA
AAAATATTTTCTGATGTGTGTTTTGATAGTGTTCAAAGAAATGTGTCTCAAATTTTCATA
ATGTATAACCATGAACAAATTTGTAAATTTCTTTCCTTTACTAACCCCTATGTTCCACATTC
25 ATACCTTTTGTTATGTCCACGGTAATGTTTTCTTTGCTCATCTTCTCCCTGTGGAGACAT
CTGAAGAATATGCAGCACACCGCCAAAGGATGCAGAGACATCAGCACCACAGTGCACATC
AGAGCCCTGCAAACCATCATTGTGTCTGTAGTGCTATACACTATTTTTTTTCTATCATTT
TTTGTTAAAGTTTGGAGTTTGTGTCAACAGAGAGATACCTGATCTTTTGTGTTGTCTGG
GCTCTGGGAAATGCTGTTTTTTCTGCTCACCCATTTGTCATGATTTTGGTAAACAGAAGA
30 TTGAGATTGGCTTCTCTCTCTGATTTTTTGGCTCTGGTACAGGTTTAAAAATATAGAA
GTATAGGGTCCAAAGACCACCAAGGAATCATTTTCCTTATCCTAAAGAAAAATCAGGAG

SEQ ID NO:131

Mouse T2R14 amino acid sequence

MLSTMEGVLLSVSTSEAVLGIVGNTFIALVNCMDYNRNKKLSNIGFILTGLAISRICLVL
ILITEAYIKIFYPQLLSPVNIIEELISYLIWIIICQLNVWFATSLSIFYFLKIANFSHYIFV
5 WLKRRIDLVFFFLIGCLLISWLFSFPVVAKMVKDNKMLYINTSWQIHMKKSELIINYVFT
NGGVFLFFMIMLIVCFLLIISLWRHRRQMESNKLGFRLNTEVHVRTIKVLLSFIILFIL
HFMGITINVICLLIPESNLLFMFGLTTAFIYPGCHSLILILANSRLKQCSVMILQLLKCC
ENGKELRDT

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SEQ ID NO:132

Mouse T2R14 nucleotide sequence

CTGCAGGTATATACCTACCCTGAAGGCTTCATCTAGAGTAAACAAAGTAGTCTGTATAGT
15 CTGCCATTCCCTCAGATTCTCCTCAACTTCCCACCCTCCAGTGACCTTTCTCCTTTTCTAC
AGTCAAACCTATGGACCTCACAACCTGACACTTCTTCAGATGCAAAATATTCTCACAGAGA
CAAGTAAACATACAAAACAAATACTTTAATTTGCCTATTAACAAATGGCAAGAAAAGAT
TCAGGCTTGAACATCCTGTAGACAAGCTAAGGACAGGAGCAACTGAAGGGATCTCCATGA
AGACCTTTTCTAGATTTCTACCAAAAGTAATTTTAACTATATTTAAGTCTTTAAAGAAAGA
20 AAGTAAAGCCACTCTTTTATTGAACAGCAATAGATTGGAATCTTAAACAACTGCAACAGA
AGCCATTTTAAAGATCAACAAAGATGCTGAGCACAATGGAAGGTGTCCTCCTTTTCTAGTTT
CAACTAGTGAGGCTGTGCTGGGCATTGTAGGGAACACATTCATTGCACTTGTAACCTGTA
TGGACTATAACAGGAACAAGAAGCTCTCTAATATTGGCTTTATTCTCACTGGCTTGGCAA
TTTCCAGAATTTGCCTTGTGTTGATCTTAATCACAGAGGCATACATAAAAATATTCTATC
25 CACAGTTGCTGTCTCCTGTCAACATAATTGAGCTCATCAGTTATCTATGGATAATTATCT
GTCAATTGAATGTCTGGTTTGCCACTAGTCTCAGTATTTTTTATTTCCTGAAGATAGCAA
ATTTTTCCCACTACATATTTGTCTGGTTAAAAAGAAGAATTGATTTAGTTTTTTTCTTCC
TGATAGGGTGCTTGCTTATCTCATGGCTATTTTCTTTCCAGTTGTTGCGAAGATGGTTA
AAGATAATAAAATGCTGTATATAAACACATCTTGGCAGATCCACATGAAGAAAAGTGAGT
30 TAATCATTAACCTATGTTTTACCAATGGGGGAGTATTTTTATTTTTTATGATAATGTTAA
TTGTATGTTTCTGTTAATCATTTCACTTTGGAGACATCGCAGGCAGATGGAATCAAATA
AATTAGGATTCAGAGATCTCAACACAGAAGTTCATGTGAGAACAATAAAAGTTTTATTGT
CTTTTATTATCCTTTTTTATATTGCATTTTCATGGGTATTACCATAAATGTAATTTGTCTGT
TAATCCCAGAAAGCAACTTGTTATTCATGTTTGGTTTGACAACCTGCATTCATCTATCCCG

GCTGCCACTCACTTATCCTAATTCTAGCAAACAGTCGGCTGAAGCAGTGCTCTGTAATGA
TACTGCAACTATTAAAGTGCTGTGAGAATGGTAAAGAACTCAGAGACACATGACAGTCTG
GAACACATGCAATCTGGAATTGTCAGTGGA AAAAGTTACTGAAGATCTTTTCACTTGAC
TATGCTCTTTTATTGATTTGGCATCATTATCAAACACTGTTGGAGCCTTGTGAACTCTTG
5 TTCAGAGTCTTCTGCCTCTCAAGGAATCACACTCC

SEQ ID NO:133

Mouse T2R15 amino acid sequence

10

MCAVLRSILTIIFILEFFIGNLGNGFIALVQCMDLRKRRTFPSADHFLTALAI SRLALIW
VLFLDSFLFIQSPLLMTRNTLRLIQTAWNISNHFSIWFATSLSIFYLFKIAIFS NYLFFY
LKRRVKRVVLVILLLSMILLFFNIFLEIKHIDVWIYGTKRNITNGLSSNSFSEFSRLILI
PSLMFTLV PFGVSLIAFLLLI FSLMKHVRKMQYYTKGCKDVRTMAHTTALQTVVAFLLLY
15 TTFFLSLVVEVSTLEMDESMLLFAKVTIMIFPSIHSCIFILKHNKLRQDLLSVLKW LQY
WCKREKTLDS

SEQ ID NO:134

20 Mouse T2R15 nucleotide sequence

AATAATAGATTTTTTAATATTCAGAATTTTTAAGTAATGTAGTATTGTTAGCAGCATAGC
TTATAGGAAAAGTTCCAAGTAATTTTGATTTTGTAATTCTGATTCCCCCAAATCAAGTAT
CAAGTTTACCTGCACAGACAAGGGAAGAAGTGGCAAAATGTGCAATGAGAGCAACTTTA
25 TTTGACTGTCAGTACGTTGAAATTCAGTGTTTCCTTAATCAGTTATGGATTGACATTTAT
GTGCACAGAACCTGGAAGAATTT CAGCCAAGCTGGAGGTAAAAATCCAAAATTCTGATGA
TAAAACCAAAGTAAATCACAGGTAAATCTTCTTTATTTTTCTTTTTTAATACTGTATAT
GGACATTTTTTAATACAGCATATTTTTTTTTTGAAATTTAGAAAAAACCACTAAGAAAT
ATTCACCAATGGAATAGACTTTAAAGTCACTTAGAGAATGTGTGCTGTTCTACGTAGCAT
30 ACTGACAATCATTTTCATTTTGGAGTTCTTCATTGGAAATCTGGGGAATGGATTCATAGC
TCTGGTACAATGCATGGACTTACGAAAGAGAAGAACGTTCCCTTCAGCAGATCATTTCT
CACTGCTCTGGCCATCTCCAGGCTTGCTCTGATATGGGTTTTATTCTAGATTCATTTCT
GTTTATACAATCCCATTACTGATGACTAGAAATACATTAAGACTGATTCAGACTGCCTG
GAATATAAGCAATCATTT CAGTATATGGTTTGCTACCAGCCTCAGCATCTTTTATCTCTT

CAAGATAGCCATTTTTCTAACTATCTTTCTTCTACCTGAAGCGGAGAGTTAAAAGGGT
 GGTTTTGGTGATACTGCTGCTATCCATGATCCTTTTGTTTTTAATATATTTTAGAAAT
 CAAACATATTGATGTCTGGATCTATGGAACCAAAGAAACATAACTAATGGTTTGAGTTC
 AAACAGTTTTTCAGAGTTTTCCAGGCTTATTTTAATTCCAAGTTTAATGTTTACATTAGT
 5 ACCCTTTGGTGTATCCTTGATAGCTTTCCTCCTCCTAATCTTTTCCCTTATGAAACATGT
 AAGGAAGATGCAGTACTACACCAAAGGATGCAAAGATGTCAGAACCATGGCCACACCAC
 AGCCCTGCAGACTGTGGTTGCCTTCCTCCTATTATATACTACTTTCTTTCTGTCTCTAGT
 TGTGGAAGTTTCAACACTTGAAATGGATGAAAGTCTGATGCTTCTGTTTGCAAAGTTAC
 TATAATGATTTTTCTTCCATCCACTCCTGTATTTTCATTTGAAACATAATAAGTTGAG
 10 ACAGGACTTGCTTTCAGTACTGAAGTGGCTACAGTATTGGTGCAAGCGTGAGAAAACCTT
 GGATTCATAGACCATTGTATGCATCACCTTGAATATTCTAGAGGGGTGTAGGTTTATATG
 AAAGTATTGAATTTTTAAATTTGAGCCTTTTGTATATTTTCT

15 **SEQ ID NO:135**

Mouse T2R16 amino acid sequence

MNGVLQVTFIVILSVEFIIGIFGNGFIAVVNIKDLVKGRKISSVDQILTALAIISRIALLW
 LILVSWWIFVLYPGQWMTDRRVSIMHSIWTFNQSSLWFATSLSIFYFFKIANFSPNIFL
 20 YLKVRLKKVMIGTLIMSLILFCLNIIIMNAPENILITEYNVMSYSLILNNTQLSMLFPF
 ANTMFGFIPFAVSLVTFVLLVFSWLKHQRKMQHSAHGCRDASTKAHIRALQTLIASLLLY
 SIFFLSHVMKVWSALLLERTLLLLITQVARTAFPSVHSWVLILGNAKMRKASLYVFLWLR
 CRHKE

25

SEQ ID NO:136

Mouse T2R16 nucleotide sequence

TTTATGATGGAAAGAATAAAACCATTAGCAAGGCTTAATGGCTTGTTTGGTATTAGACCT
 30 GTACATTGTTTATGGAACATGATATGGAGCTTTGTTTATTGAATATGCACAATATTTTAG
 AAGCATGTTTCAAAGAATCTTAAGTAATTACAATAGAAATTGAAGCATCCAAGTGAAGAT
 GAATGGTGTCTACAGGTTACATTTATAGTCATTTTGAGTGTGGAATTTATAATTGGCAT
 CTTTGGCAATGGATTCATAGCGGTGGTGAACATAAAGGACTTGGTCAAGGGAAGGAAGAT
 CTCTTCAGTGGATCAGATCCTCACTGCTCTGGCCATCTCCAGAATTGCACTGCTGTGGTT

AATATTAGTAAGTTGGTGGATATTTGTGCTTTACCCAGGACAATGGATGACTGATAGAAG
 AGTTAGCATAATGCACAGTATATGGACAACATTCAACCAGAGTAGTCTCTGGTTTGCTAC
 AAGTCTCAGCATCTTTTATTTTTTCAAGATAGCAAATTTTTCCAACCCTATTTTTCTTTA
 TTTAAAGGTCAGACTTAAAAAGTCATGATAGGGACATTGATAATGTCTTTGATTCTCTT
 5 TTGTTTAAATATTATCATTATGAATGCACCTGAGAACATTTTAATCACTGAATATAATGT
 ATCTATGTCTTACAGCTTGATTTTGAATAACACACAGCTTTCTATGCTGTTTCCATTTGC
 CAACACCATGTTTGGGTTTCATACCTTTTGCTGTGTCACTGGTCACTTTTGTCTTCTTGT
 TTTCTCCCTGTGGAAACATCAGAGAAAGATGCAACACAGTGCCCATGGATGCAGAGATGC
 CAGCACTAAGGCCACATCAGAGCCTTGCAGACATTGATTGCCTCCCTCCTCCTGTATTC
 10 CATTTTCTTCCTGTCTCATGTTATGAAGGTTTGGAGTGCTCTGCTTCTGGAGAGGACACT
 CCTGCTTTTGATCACACAGGTTGCAAGAACAGCTTTTCCGTCAGTGCACTCCTGGGTCCT
 GATTCTGGGCAATGCTAAGATGAGAAAGGCTTCTCTCTATGTATTCCTGTGGCTGAGGTG
 CAGGCACAAAGAATGAAACCCTACAGTGACAGACCTGGGGTATATTTATGTGGATGATC
 TTACATATCTTAGAGGAAAATGGATTAAAAGAAATTCTCATATTTATAAATTTTTAGGTC
 15 TGAATTACATAAAAATGTATATAATATTTTCAAAGTACAAGATAGTAGTTTATAACTTAC
 ATGATAAATACTGTCTATGCATCTTCTAGTCTTTGTAGAATATGTAAAAACATGTT

SEQ ID NO:137

20 Mouse T2R17 amino acid sequence

MKHFWKILSVISQSTLSVILIVELVIGIIGNGMVLVHCMDWVKKKKMSLVNQILTALSI
 SRIFQLCLLFISLVINFSYTDLTSSRMIVMYNAWILANHFSIWIATCLTVLYFLKIAN
 FSNSFFLYLKWRVEKVSVTLLVSLLLLILNILLTNLETDMWTNEYQRNISCSSFSSHYA
 25 KCHRQVLRHLHIIFLSVPVVLSTFLLLIIFSLWTHHKRMQQHVQGRDARTTAHFKAQT
 VIAFFLLYSIFILSVLIQIWKYELLKKNLFVVVFCEVVYIAFPTFHSYILIVGDMKLRQAC
 LPLCIIAAEIQTTLCRNFRSLKYFRLCCIF

30 **SEQ ID NO:138**

Mouse T2R17 nucleotide sequence

GAATTCTGGTCTGGCACCCCTGAGCTGTGTGAGTAGACACATTATCATGGAAAGAGATTC
 AGAATCTGTCACTGTCAAACTGCATGTTTGCTCCTCTGTTAGTGTGTTGGGGAAAGTTA

AGAAAAATACATTTTATGAGAATCAACTCAGAGGTTGTCAGAAATTGTCGAAACAGCATT
 TTAAAAATTTACATCTCAACTGGATATATGAGCAAGTCTTTATAACTGATATATAAAATG
 AAGCACTTTTGAAGATATTATCTGTTATCTCCCAGAGCACACTTTTCAGTCATTTTAATC
 GTGGAATTAGTAATTGGAATTATAGGAAATGGGTTTCATGGTCCTGGTCCACTGTATGGAC
 5 TGGGTTAAGAAAAAGAAAATGTCCCTAGTTAATCAAATTCCTTACTGCTTTGTCAATCTCC
 AGAATTTTTCAGCTCTGTTTATTGTTTATAAGTTTAGTAATCAACTTTTCATATACAGAT
 TTAATAACAAGTTCAAGGATGATACAAGTCATGTACAATGCTTGGATTTTAGCCAACCAT
 TTCAGCATCTGGATTGCTACATGCCTCACTGTCCTTTATTTTCTAAAGATAGCCAATTTT
 TCTAACTCTTTTTTTCTTTATCTAAAGTGGAGAGTTGAAAAAGTAGTTTCAGTTACACTG
 10 TTGGTGTCAATTGCTCCTCCTGATTTTAAATATTTTACTAACTAACTTGGAAACCGACATG
 TGGACAAATGAATATCAAAGAAACATATCATGCAGCTTCAGTTCTCATTACTATGCAAAG
 TGTCACAGGCAGGTGTTAAGGCTTCACATTATTTTCCTGTCTGTCCCCGTTGTTTTGTCC
 CTGTCAACTTTTCTCCTGCTCATCTTCTCCCTGTGGACACATCACAAGAGGATGCAGCAG
 CATGTTTCAGGGAGGCAGAGATGCCAGAACCACGGCCCACTTCAAAGCCCTACAACTGTG
 15 ATTGCATTTTTCCTACTATATTCCATTTTATTCTGTCTGTCTTAATACAAATTTGGAAA
 TATGAATTACTGAAGAAAAATCTTTTCGTTGTATTTTGTGAGGTTGTATATATAGCTTTT
 CCGACATTCCATTCATATATTCTGATTGTAGGAGACATGAAGCTGAGACAGGCCTGCCTG
 CCTCTCTGTATTATCGCAGCTGAAATTCAGACTACACTATGTAGAAATTTTAGATCACTA
 AAGTACTTTAGATTATGTTGTATATTCTAGACAAAAATTAAGTATACAAATGTCTTTTG
 20 TATTTTTCATTTTAAATATCCTTTAATTTTGACTGCATGAAATTGATTTCTGCTTGCAAT
 TATCACTGATTAAACTATTAATAATTTAACTAG

SEQ ID NO:139

25 Mouse T2R18 amino acid sequence

MVPTQVTIFSIIMYVLESLVIIIVQSCTTVAVLFRWMMHFQRLSPVETILISLGISHFCLQ
 WTSMLYNFGTYSRPVLLFWKVSVVWEFMNILTFWLTSWLAVLYCVKVSSFTHPIFLWLRM
 KILKLVLWLILGALIASCLSIIPSVVKYHIQMELVTLNLPKNNSLILRLQQFEWYFSNP
 30 LKMIGFGIPFFVFLASIIILLTVSLVQHWVQMKHYSSSNSSLKAQFTVLKSLATFFTFFTS
 YFLTIVISFIGTVFDKKSFWVCEAVIYGLVCIHFTSLMMSNPALKKALKLQFWSPEPS

SEQ ID NO:140

Mouse T2R18 nucleotide sequence

GCGTGCTTCACAGAGCAGTATACTACAAAGCAAATGTCATTGCTGCCATTGTATATTTCT
CTAAAGACATTTACATTTTATCTCCCTGTCCCATTTGTGTGCAGAGCCCACACTTCAATC
5 AATCAATTCCTTAATTATAAGCTATTGTTTCATTATTTCAATTCCTACGTTTTTTTGCAT
TTTTACTAAAACCTCAAAGCAGACATTTTCTAATTATAATCCTACATGTAGTTAGAATTT
TAAAAATTATATACTATTTTCTTTGCACCACTGAGTTCAGTAGGTTTTGAAGGTTTATGC
TTAACAATTGAACATTTTCATGTTAGATTATTCCTGCCTTCCTAATCCTGAATAATTAAAT
GTCCATCCAGGCTTAGAATTCACAGAGTCAACAGCTTTCACCTTGATTCTCTCACTATCT
10 ATCAATGACTAGAATCTGTCTGTCACTTTTGAAACCGCTAATTAAATAGTTGGTGCTTAT
TTAAAGGGTGCCCCATGCCAAGAGAAAATGTATTTCTTCTCTAGATGCCTTCGTCCTTTA
CAAGTTACATGCTTTACTGATGGTGAATTGGTTTTCTTCCAGTTCATCTGGGTAAAGTGA
CCTAAGAACCTAGCCATGGAAGGAGAAACAGAAGCAAATATTAACGATACAAGAACAAGT
TCCAGAACATTGGAAAGTACTTAGTAAAGGCATTGGAATTAGCAAAAGAATAGTAGCGAA
15 GCAAAAATACTTCATCTCCATTGGGAGGTCAAGAAAGACTATGCAGTGTTTTTGATGCA
ACTTGTCATCTCTGAGTTAGACGATTCAGCACACACTTTTGAGATTGAACTTCAACAGGT
GGAGCCAGCAGACCTGAGCTTTAGGAATGATGGTGGAATTTCCAAGCAAAGACTTCCGTT
ACCTTTTTGATGTCCCCTAACAATTCGGTTGCAATGCTCACACCGCCCAACTGTTGAAAT
GCTTGGGAAAAGGGATTCTGAGACTGGCATTAGTATGTCATTTGACAGAATGGAAACATT
20 GCCCAGGGCATTAAATGCACAGTAAAGGATTCACCTTTTCTAAGTGCTCAAATTTTAAATT
TGnATATTTTTTAGAAGACATTATTTAAAAGAAAGGTGGAGAGGATATCCAAACAGCACCT
TGAGCAGATAAAGAGGTGAAGAAGAAAAACAACATGCGTACATGATGGATTTCTCTTTA
TGAAAATGATCAAATGATCTTAGGATCAAGAATCCACACCTGAATGAGATTTGCTTGTAT
CCCTGTGTGAATTTGACCTAACAAGCAAAGCACAGACAAATGCTGTAGATAGGGAAATGT
25 CTATGTCAAATGTGTGTAAGGAGGATTTGCATCCACAAAGAAGTGCCCTCTTATACTGAG
AGTGCTAAGAACACATGTCCGTTTCATATTCGGAAAGTGGTATAGAGCTGTTGAGTCTTT
GGCTAGGAAGAGACTTCAGAGTGGAAGC**ATGGTGCCAACGCAAGTCACCATCTTCTCCAT**
CATCATGTATGTGCTTGAGTCCTTAGTAATAATTGTGCAAAGTTGCACAACGGTTGCAGT
GCTATTCAGAGAGTGGATGCACTTTCAAAGACTGTCACCGGTGGAGACGATTCTCATCAG
30 **CCTGGGCATCTCACATTTCTGTCTACAGTGGACATCAATGCTATACAACCTTTGGTACTTA**
TTCTAGGCCTGTCCTTTTATTTTGGAAGGTATCAGTCGTCTGGGAGTTCATGAACATTTT
GACATTCTGGTTAACCAGTTGGCTTGCTGTCCTCTACTGTGTCAAGGTCTTTCCTTCAC
TCACCCCATCTTCCTCTGGCTGAGGATGAAAATCTTGAACTGGTTCTCTGGTTGATACT
GGGTGCTCTGATAGCTTCTTGTTTGTCAATCATCCCTTCTGTTGTTAAATATCACATCCA

GATGGAATTAGTCACCCTAGATAATTTACCCAAGAACAATTCTTTGATTCTAAGACTACA
 ACAGTTTGAATGGTATTTTTCTAATCCTTTAAAAATGATTGGCTTGGTATTCCTTTCTT
 CGTGTTCTGGCTTCTATCATCTTACTCACAGTCTCATTGGTCCAACACTGGGTGCAGAT
 GAAACACTACAGCAGCAGCAACTCCAGCCTGAAAGCTCAGTTCAGTCTGTTCTGAAGTCTCT
 5 TGCTACCTTCTTCACCTTCTTCACATCCTATTTTTCTGACTATAGTCATCTCCTTTATTGG
 CACTGTGTTTGGATAAGAAATCTTGGTTCTGGGTCTGCGAAGCTGTCATCTATGGTTTAGT
 CTGTATTCACTTCACTTCACTGATGATGAGCAACCCTGCATTGAAAAAGGCACTGAAGCT
 GCAGTTCTGGAGCCCAGAGCCTTCCTGAGGCAGGAAACACAGTTAAGCCTCTAGGGTAAG
 GAGACTTTGCATTGGCACAGTCCCTATAGTGTAATGCAAACCTGAACACAAACTTCATCC
 10 CTTTTACATCCACAAATGGCTGCATCTATACATCATCACCAGTCTTCCCTGTATTCTGA
 CCCATTCTCTTCTGCTATCCATAGTCCCCAGGTTGGTTTTGATTTTTCTCATGATCA
 CACCAACTCTGCTTAGCTTTTGCCACCACTGTAATAGTAAACATGGGGTGTTCTATATAT
 TACAGTCAAAATCATTTCTCACATTGTTGATTGCCTCACAAATTCATATAAATCCCCCTTC
 CTGTCAGGAATTTATTGTCTGCTCACTTAATGCTCACCATATATTAAAGCCATTAATTCC
 15 CCCTTCCTACCTTGAGTTTAAGAAGGAAAATGTCTTACCATTGCCCACAACTATTCTGC
 TGCTTCTAGACTTTTATGCAAGTGATTTATACACACACACACACACACACACATAC
 AAACAAC

20 **SEQ ID NO:141**

Mouse T2R19 amino acid sequence

MMEGHMLFLLV VVVVQFLTGVLANGLIVV VVNAIDLIMWKKMAPLDLLLFCLATSRIILQL
 CILFAQLGLSCLVRHTLFADNVT FVYIINELSLWFATWLG VFYCAKIATIPHPLEFLWLKM
 25 RISRLVPWLILASVVYVTVTTFIHSRETSELPKQIFISFFSKNTTRVRPAHATLLSVFVF
 GLTLPFLIFTVAVLLLLSSLWNHSRQMR TMVGTREPSRHALVSAMLSILSFLILYLSDM
 VAVLICTQGLHFGSRTFAFCLLVIGMYP SLHSIVLILGNPKLKRNAKTFIVHCKCCHCAR
 AWTSRNPRLSDLPVPATHHSANKTSCSEACIMPS

30

SEQ ID NO:142

Mouse T2R19 nucleotide sequence

CTGCAGCCTAGAGAACTAATGCATAGGAACTTATATTCCCACCTCCGTGACGTCACTCT
 GACAGAAGTGAAGTTATATTCCCACCTCCGTGACGTCACTCTGACAGAAGTGACTTGTTT
 TTGTATGATGCTCCAGGATGCCTCATTAGCATTGAGGACAATCATAATTAAGTAAGGCAA
 GGCATGAAGGTGGTCCTCACTAGGTACCTGGAGGCTTCTGGTTGCATGATTTACTTGTGA
 5 TGACTCTGACACTTAAGAAGACCTGAAAAATGCAAAGCTGTCATAAGGCACAGTTCGTT
 TCTATGGTATCTCTTCCTTATTTGACTGACATTGAGTTGAGAAGGCAGCACTATAAACAA
 ATGGGCCCCACCTTCCTCTTCCATTGTCTTTGGGTGGCATCATCTCCAAAGGAACCTTG
 GTCTAGTTGAAAGAAGCCAGAAATCATACATGGCTGAGACTGTGCATAACTCTATGTATC
 ATTTAAAGAAGTCATTGGTTCTTCTTATTTTAAATGATGGAAGGTCATATGCTCTTCTT
 10 CCTTCTGGTTCGTGGTAGTGCAGTTTTTAACTGGGGTCTTGGCAAATGGCCTCATTGTGGT
 TGTCAATGCCATCGACTTGATCATGTGGAAGAAAATGGCCCCACTGGATCTGCTTCTTTT
 TTGCCTGGCGACTTCTCGGATCATTCTTCAATTGTGTATATTGTTTGCACAGCTGGGTCT
 ATCCTGTTTGGTGAGACACACGTTATTTGCTGACAATGTTACCTTTGTCTACATTATAAA
 CGAACTGAGTCTCTGGTTTGCCACATGGCTTGGTGTCTTCTACTGTGCCAAGATTGCTAC
 15 CATCCCTCACCCACTCTTTCTGTGGCTGAAGATGAGGATATCCAGGTTGGTGCCATGGCT
 GATCCTGGCATCTGTGGTCTATGTAAGTGTACTACTTTTCATCCATAGCAGAGAGACTTC
 AGAACTTCCTAAGCAAATCTTTATAAGCTTTTTTTCTAAAAATACAACCTCGGGTCAGACC
 AGCGCATGCCACACTACTCTCAGTCTTTGTCTTTGGGCTCACACTACCATTTCTCATCTT
 CACTGTTGCTGTTCTGCTCTTGTGTCCTCCCTGTGGAACCACAGCCGGCAGATGAGGAC
 20 TATGGTGGGAAGTAGGGAACCTAGCAGACATGCCCTCGTCAGTGCGATGCTCTCCATTCT
 GTCATTCCCTCATCCTCTATCTCTCCCATGACATGGTAGCTGTTCTGATCTGTACCCAAGG
 CCTCCACTTTGGAAGCAGAACCTTTGCATTCTGCTTATTGGTTATTGGTATGTACCCCTC
 CTTACACTCGATTGTCTTAATTTTAGGAAACCTAAGCTGAAACGAAATGAAAAACGTT
 CATTGTCCATTGTAAGTGTGTCATTGTGCAAGAGCTTGGGTCACCTCAAGGAACCCAAG
 25 ACTCAGCGACTTGCCAGTGCCTGCTACTCATCACTCAGCCAACAAGACATCCTGCTCAGA
 AGCCTGTATAATGCCATCTTAATTGTCCAACCTGAGGCTTAATCATTTCAAAGGGTAAAT
 TGATGATCAAAGCCCAACACATGATATGACATCAAGGTCCATATCCCAGTAGTCATGTGG
 AAATACCACCTTGCAAAATGATGTCATTGAGAAACCAGGGCAAATGGAGTCTAGGTCTTT
 CAGTATGATTTGCTGCAG

30

SEQ ID NO:143

Mouse T2R20 amino acid sequence

MNLVEWIVTIIIMMTEFLLGNCANVFITIVNFIDCVKRRKISSADRIITAIAIFRIGLLWA
MLTNWHSVFTPDTDNLQMRVFGGITWAITNHFTTWLGTILSMFYLFKIANFSNSLFLHL
KRKLDNVLLVIFLGSSLFLVAYLGMVNIKKIAWMSIHEGNVTTKSKLKHVTSITNMLLFS
LINIVPFGISLNCVLLLIYSLSKHLKNMKFYGKGCQDQSTMVHIKALQTVVSFLLLYATY
5 SSCVIIISGWSLQNAPVFLFCVTIGSFYPAGHSCILIWGNQKLKQVFLLLLRQMRC

SEQ ID NO:144

Mouse T2R20 nucleotide sequence

10

CTAGATGGGCTGTTTCATATAATGACTGGAACCTCCCTACATGCTCCACGTCTTGAGTTCT
AAAATTTCACTAACAAATTTTTGACTGCCATAAATAATGAAGGTTTAAAGAAAGAACAAC
ATTTGAAGCAATGGACCAGAATTCCTCTTTATTTGACTCTTAGCAAATTGGAATGCAGCA
TCCTTTCAAGAGCAGCACTGAAATATAACCAGTCAATGGCAGAGAGTAAAAAAGTATGCAA

15

TTGGAGACATTATGGTAATATAAATTTCCATTAAAAATGAGACTGCATTACCTATTACA
ACACATTGCTATTCTGCTCAACACAGAGTTAAAAAGAAACAAGAACTCTTGTATACATTC
AGTTAGTCACAAGTATAATTATGTTACATATTTTAAAAAATGAATCATGATCTGTGAA
TTGAGCCTGGCTTTTTTTGTCTCTCTCTTTTTATTCTTTTCCTTTAGACAGACACA**ATGA**
ATTTGGTAGAATGGATTGTTACCATCATAATGATGACAGAATTTCTCTTAGGAACTGTG

20

CCAATGTCTTCATAACCATAGTGAACCTCATCGACTGTGTGAAGAGAAGAAAGATCTCCT
CAGCTGATCGAATTATAACTGCTATTGCCATCTTCAGAATTGGTTTGTGTTGGGCAATGT
TAACGAACTGGCATTACATGTGTTTACTCCAGACACAGACAATTTACAAATGAGAGTTT
TCGGTGGAATTACCTGGGCTATAACCAACCATTTTACCACTTGGCTGGGGACCATACTGA
GCATGTTTTATTATTCAAGATAGCCAATTTTCCAACAGTCTATTTCTTCATCTAAAAA

25

GAAAACTTGACAATGTTCTACTTGTGATTTTCCTGGGATCGTCTCTGTTTTTGGTTGCAT
ATCTTGGGATGGTGAACATCAAGAAGATTGCTTGGATGAGTATTCATGAAGGAAATGTGA
CCACAAAGAGCAAACCTGAAGCATGTAACAAGCATCACAAATATGCTTCTCTTCAGCCTGA
TAAACATTGTACCATTTGGTATATCACTGAACTGTGTTCTGCTCTTAATCTATTCCCTGA
GTAACATCTCAAGAATATGAAATTCTATGGCAAAGGATGTCAAGATCAGAGCACCATGG

30

TCCACATAAAGGCCTTGCAAACCTGTGGTCTCTTTTCTCTTGTATATGCCACATACTCTT
CCTGTGTCATTATATCAGGTTGGAGTTTGCAAATGCACCAGTCTTCCTGTTTTGTGTGA
CAATTGGATCCTTCTACCCAGCAGGTCATTCTTGTATCTTGATTGGGGAAACCAGAAAC
TAAACAGGTCTTTCTGTTGTTGCTGAGGCAGATGAGATGCTGACTGAAAAAATGAAAGT
CCCCCTGTCTCTAG

SEQ ID NO:145

Mouse T2R21 amino acid sequence

5

MGSNVYGILTMVMIAEFVFGNMSNGFIVLINCIDWVRKGTLSIGWILLFLAISRMVLIW
EMLITWIKYMKYSFSFVTGTELRGIMFTWVISNHFSWLATILSIFYLLKIASFSKPVFL
YLKWREKKVLLIVLLGNLIFLMLNILQINKHIEHWMYQYERNITWSSRVSDFAGFSNLVL
LEMIVFSVTPFTVALVSFILLIFSLWKHLQKMHLNSRGERDPSTKAHVNALRIMVSFLLL
10 YATYFISFFLSLIPMAHKTRLGLMFSITVGLFYPSSHFILILGHSNLRQASLWVMTYLK
CGQKH

SEQ ID NO:146

15 Mouse T2R21 nucleotide sequence

CTCTTTTGAAGACAATAGTTGTTCTACTAGCTATTGATAGCATGTTTACATTTGTCATTT
TCAAGTATGTTTCAGAAACAAAGCTACATATTGTGGGGAGTATATAAAATATGAAAGCATG
CCATTCCCAGGCATCCAAGGATCCCTGTGTATTAAAAGGCAACAAAGCAGAACCAAATGT
20 TCTGTTTTGGACATGAGCTTCTTCCAATTCAACTGCTGAAAAATTTGGATAACTACATAT
AAAAC TAAGAACACAGAGTGTCACAGAGCAGTCTCTGCTCTCCAATTCACCAGGATTAAT
ATTGACAGACCCAAAAGATGTCATTTAGGTAAATTTTGGATGAATCATATTGTTGTCACC
TTTGTGCTCTAGAACATAAGCTGATAGAATCAAATTTTCTTTAGCAGAGACAATGCAAAT
TGATATAACAGTGAAAGAGAATATATCTTTATTTGCATGTTAGCAAATGACAGCTGGATG
25 CACTTCATGATTTTCTGCAATCTAGTTCAGTCTTTAGAAGGATATATATATATATATATA
TATATATATATATATATATATATATATATATATAAACCTTAGTCTTGAAAGATATCAGAA
AGAAGGATTTACAGAATGTACAGAGCCATTAGCAAAATTTTAATATACTCATCGACAT
TAGGTCAGTCACTACATAAGAAGGACTTGAATGAAAGCTTATCTTAGTTTTTGAGACTAC
AGGGACATTTACCTTGCCAAATGAGAAGCAGTGAGTCTTCTTTGTCTGGACATGGGAAG
30 CAATGTGTATGGTATCTTAACTATGGTTATGATTGCAGAGTTTGTATTTGGAAATATGAG
CAATGGATTCATAGTGCTGATAAACTGCATTGATTGGGTCAGGAAAGGAACCTTTTCTTC
CATTGGTTGGATCCTGCTTTTCTTGGCCATTTCAAGAATGGTGTGATATGGGAAATGTT
AATAACATGGATAAAATATATGAAGTATTCATTTTCATTTGTGACTGGAACAGAATTACG
GGGTATCATGTTTACCTGGGTAATTTCCAATCACTTCAGTCTCTGGCTTGCCACTATTCT

CAGCATCTTTTATTTGCTCAAATAGCCAGTTTCTCAAACCGGTTTTTCTCTATTTGAA
 GTGGAGAGAGAAGAAAGTGCTTCTGATTGTCCTTCTGGGAAATTTGATCTTCTTGATGCT
 CAACATATTACAAATAAACAAACATATAGAACACTGGATGTATCAATATGAGAGAAATAT
 AACTTGGAGTTCTAGAGTGAGTGACTTTGCAGGGTTTTCAAATCTGGTCTTATTGGAGAT
 5 GATTGTGTTCTCTGTAACACCATTACAGTGGCCCTGGTCTCCTTCATCCTGTTAATCTT
 CTCCTTGTGGAAACATCTACAGAAAATGCATCTCAATTCTAGAGGGGAACGAGACCCAG
 CACTAAAGCCCATGTGAATGCCTTGAGAATTATGGTCTCCTTCCTCTTACTCTATGCCAC
 TTACTTCATATCTTTTTTTCTATCATTGATTCCCATGGCACATAAAACACGACTGGGTCT
 TATGTTTAGCATAACTGTTGGGCTTTTCTACCCTTCAAGCCACTCATTATCTTAATTTT
 10 GGGACATTCTAATTTAAGGCAAGCCAGTCTTTGGGTGATGACATATCTTAAATGTGGGCA
 AAAGCATTAGAATTTCACTATTCCATAAGGCAGCCAAACCACGTGCTACTAGGTATATGA
 TACTACTCAGTGGTAAAGCCCTAGGCAAACATTAACCTTAGAAAATATATAATTTTGTGA
 CTCTTCTGTATTTGATAAATCACTCACATATTTAGAAGAATGCTACAGTAGTGTGATCTT
 GTACATGATTGTAACAATTCAATTTTATTAATATAGTTCAGGCATGATAACATACCCCTG
 15 ATAAGTAAAAGTAAGTAGGATGCTACATATATATTTAGATCTAGACTTAGGGGCAAAGA
 GAGACCCAGCTGATAGCTGTGCAATAAAGATTTTAATTTTCATCCTGTTGTGAGTTATCT
 GAAATCTATGTCACTGAAGGCATAAGCAAGATTTTCACACACTGAAACAATCTCTTATGC
 TTTCTTATATTGTTTTAAAGTAAATTAGAAAATTTAAATAAACTTAATGGCAATTGAAA
 TTACAAAAGCTAAACACATGTGGTTATTAGAAATTAGACTGTATGTAGGTCCTAGGGGAT
 20 GGCTTAGTAAAGTGCTTTGTTGCAAGCTTCAGGATATGATTCTAAATCCCTAGATTCAAT
 TAAAAACCTGGCATAAATAGCCAATGTAAAATTTGTCTGTAAAATGTAACCAGTGCTAAG
 AGTACCAAGACAACAAAATGTTTACTTTTAAAACCATTTATTGATATTCTTTTAAAATA
 GGTATGTATTTTACTATTTAAATAAGATTTTGTCAAAGCTAGTCTTGACACCTTAGGTA
 AACATAGGAAGGCAACAAGTTTGAAGTCAGCTACTGGGGACAGTGCTGCTAGCAGCTGAC
 25 AGAGGCCACTGCTGACTACAGCAGATCATTTACAGGTTTCAGCACTAG

SEQ ID NO:147

Mouse T2R22 amino acid sequence

30 MSSLLEIFFVVIISVVEFIIIGTLGNGFIVLINSTSWFKNQKISVIDFILTWLAISRMCVLW
 TTIAGASLRKFYKTLSSKNFKFCFDIIWTGSNYLCIACCTCISVFYLFKIANFSNSIFF
 WIKQRIHAVLLAIVLGTLMYFILFLIFMKMIANNFIYKWKLEQNTTFPVLDTLSGFLVY
 HSLYNGILIFFFIVSLTSFLLLI FSLWSHLRRMKLQGIHTKDISTEAHIKAMKTMMSFLL

FFIIYYISNIMLIVASSILDNVVAQIFSYNLIFLYLSVHPFLLVLWNSKLKWTFAQHVLRK
LVCHCGGYS

5 **SEQ ID NO:148**

Mouse T2R22 nucleotide sequence

AAATGAATAATTCATGCAAAGGATACCATTAGAATATGATCACTATTTAAATTTTAGCA
AATACATATTCAAATACCAGCACAAATGTTTCAAATTTAAAATATAAACATTATAAAACCC
10 AGCAGAGAACAAAATGATAGCCTTGATAATTGTTGGTTTGCTCAAGAAAAATGGGTGTAT
ACTTTAACATTTAATTGGGAACCTCAGTTGAGAGCATACATTTAGGGTTTTACAGAGGTAT
TCATTGCCCATTTAAGATTTGGATTACACATCTACATCAATGTGGCTGTAATCCATTTT
CCCATGATGAAATAAGGTAGAGACTGCCTATTAAACGACATGTCGAGCCTACTGGAGATT
TTCTTTGTGATCATTTTCGGTTGTAGAATTCATAATAGGAACTTTGGGAAATGGATTTATT
15 GTCCTGATAAACAGTACTTCTTGGTTCAAGAATCAGAAAATCTCTGTAATTGATTTTATT
CTTACTTGGTTGGCCATCTCCAGAATGTGTGTTCTATGGACAACAATTGCTGGTGCCTCT
CTCAGGAAATCTACAAGACGTTAAGTTACTCTAAGAATTTCAAATTTTGTTTTGACATT
ATCTGGACAGGATCCAACATTTTATGCATAGCCTGTACAACGTGCATCAGTGTCTTCTAC
TTGTTCAAGATTGCCAACTTTTCTAATTCCATTTTCTTCTGGATTAAACAGAGAATTCAT
20 GCAGTACTTCTGGCTATTGTCCTAGGCACACTCATGTATTTTATTTTCTCATTTTT
ATGAAAATGATAGCTAATAATTTTATCTACAAATGGACAAAATTGGAACAAAACACAACA
TTCCCTGTTTTAGATACTCTAAGTGGTTTCTTAGTCTACCATAGCCTCTACAATGGGATT
CTCATTTTCTTTTTTATAGTGTCTCTGACCTCATTTCTTCTTTTAATCTTCTCTTTATGG
AGCCACCTTAGGAGGATGAACTACAGGGCATAACATAAGACATAAGCACAGAAGCA
25 CACATAAAAGCTATGAAACTATGATGTCATTCCTTTTGTTCCTTCATCATATATTATATT
AGCAACATTATGCTTATTGTGGCAAGCTCCATTCTTGACAATGTGGTTGCACAAATTTTC
TCTTATAACCTAATATTTCTGTATTTATCTGTTTCATCCTTTTCTTCTGGTTTTATGGAAC
AGCAAATTGAAATGGACATTCCAGCATGTATTGAGAAAGCTGGTGTGTCATTGTGGAGGT
TATTCTTGATTTTCTAGTAAATACACTCAATATAACTGATGGATTTCTAAGGTAAGAAAAAT
30 GGAACAAGGAATAAAGAGGAGAAATATATTCCTTTTCAGATCATCTGCTCTGTCATTCTG
TCCTTAGCATGCTATTAAGAATTGTTGACTAAATCCAGTCATTTTAAACATGAGGAAAGG
ATGTTTCAATCCAACCTAGAGAGGGTACAAAATAGTCCTAGGAGGCAG

SEQ ID NO:149

Mouse T2R23 amino acid sequence

5 MFSQKINYSHLFTFSITLYVEIVTGILGHGFIALVNIMDWVKRRRISSVDQILTALALTR
FIYVLSMLICILLFMLCPHLPRRSEMLSAMGIFWVNSHFSIWLTTC LGVFYFLKIANFS
NSFFLYLKWRVKVILIIILASLIFLTLHILSLGIYDQFSIAAYVGNMSYSLTDLTQFSS
TFLFSNSSNVFLITNSSHVFLPINSLEMLIPFTVSLVAFMLLIFSLWKHHKMQVNAKQP
RDVSTMAHIKALQTVFSFLLLYAIYLLFLIIGILNLGLMEKIVILIFDHISGAVFPISHS
FVLILGNSKLRQASLSVLPCLRCQSKDMDTMGL

10

SEQ ID NO:150

Mouse T2R23 nucleotide sequence

15 AATTTTCAGCAACCAATATGTAGACTGCTTAAATGCATCAGAAACATTATAAATTGAAGC
ATGTTTTTCACAGAAAATAAACTACAGCCATTTGTTTACTTTTTCAATCACCTTGTATGTG
GAAATAGTAACGGGAATCTTAGGACATGGATTCATAGCATTAGTGAACATCATGGACTGG
GTCAAAGAAGAAGGATCTCTTCAGTGGATCAGATTCTCACTGCTTTGGCCCTTACCAGA
TTCATTTATGTCTTGTCTATGCTGATTTGCATATTGTTATTTCATGCTGTGCCACATTTG
20 CCTAGGAGATCAGAAATGCTTTCAGCAATGGGTATTTTCTGGGTAGTCAACAGCCATTTT
AGCATCTGGCTTACTACATGCCTCGGTGTCTTTTATTTTCTCAAGATAGCCAATTTTTCT
AACTCTTTTTTTCTTTATCTAAAGTGGAGAGTTAAAAAGTGATTTTAATAATAATCCTG
GCATCACTGATTTTCTTGACTTTACACATTTTATCTTTAGGGATATATGATCAGTTCTCA
ATTGCTGCTTATGTAGGAAATATGTCTTATAGTTTGACAGATTTAACACAATTTTCCAGT
25 ACTTTCTTATTCTCCAACATCAATGTTTTCTTAATCACCAACTCATCCCATGTTTTC
TTACCCATCAACTCCCTGTTTCATGCTCATAACCCTTCACAGTGTCCCTGGTAGCCTTTCTC
ATGCTCATCTTCTCACTGTGGAAGCATCACAAAAGATGCAGGTCAATGCCAAACAACCT
AGAGATGTCAGTACTATGGCCACATTAAAGCCTTGCAAACCTGTGTTCTCCTTCCTGCTG
CTGTATGCCATATACTTACTTTTCCTTATCATAGGAATTTTGAACCTTGGATTGATGGAG
30 AAAATAGTGATACTGATATTTGACCACATTTCTGGAGCAGTTTTTCTATAAGCCACTCA
TTTGTACTGATTCTGGGAAACAGTAAGCTGAGACAAGCCAGTCTTTCTGTGTTGCCTTGT
CTAAGGTGCCAGTCCAAAGATATGGACACCATGGGTCTCTAGTAAATTCCAGAGTACATT
TTGTAAAAATCTTGAGGATGATCAGTTCATAGAAAAAGTTACCTTATGGGGGAAAATAA
AAAGTGGGGCTTCAATCCTGGGAGTAATAATACACAGGAGGGTAGGACAGCATGAAGGAG

ACTAGCACTATATAAGTGGTCTCATAcAGGATATGGGAAAGGAAAGATTTATGCAATAAA
GAGGGAGATCATATTGGAGGATGAGGAGGCATTACATATGTAAAATGACTATAAGAATGG
AATCATGCTAATCTAAAAAAATCTGTAATGCATTTTCATTCAGACTATATACATATATGCC
TATATATGGATATATGGGGATATATATTCTATACATATTTTAAAAGAACCTTTCTTATAT

5 AG

SEQ ID NO:151

Mouse T2R24 amino acid sequence

10

MVPVLHSLSTIILIAEFVWGNLSNGLIVLKNCIDWINKKELSTVDQILIVLAISRISLIW
ETLIIWVKDQLISSITIEELKIIIVFSFILSSHFSWLATALSIFYLFRI PN CYWQIFLYL
KWRIKQLIVHMLLGSFLVFLVANMIQITITLEERFYQYGGNTSVNSMETEFSILIELMLFN
MTMFSIIPFSLALISFLLLI FSLWKHLQKMPLNSRGDRDPSATAHRNALRILVSFLLLYT
15 IYFLSLLISWVAQKNQSELVHIICMITSLVYPSFHSYILILGNYKLKQTS LWV MRQLGCR
MKRQNTPTT

SEQ ID NO:152

20 Mouse T2R24 nucleotide sequence

25

CAAAGAGGAGAAATATTTAGCTACACAGTGTACCACATACAAGCCGTTCAATCAGTATAA
GGGGAGCAGTCATATAGAATTTGGGCTTTCTTTCTTTTAATATGGTACCTGTTCTGCACA
GTCTCTCCACCATCATACTAATTGCAGAGTTTGTTTGGGGAAATTTGAGCAATGGTTTGA
TAGTGTTGAAGAACTGCATTGACTGGATCAATAAAAAAGAGCTCTCCACAGTTGATCAAA
TACTCATTGTCTTGGAATTTCAAGAATTAGTCTCATCTGGGAAACACTAATTATATGGG
TTAAAGATCAACTAATTTTCATCTATTACTATTGAAGAATTAAAAATAATTGTGTTCAGCT
TTATACTATCTAGCCACTTCAGTCTCTGGCTTGCTACAGCTCTCAGCATCTTCTATTTAT
TCAGAATACCTAATTGCTACTGGCAGATCTTTCTCTACTTGAAATGGAGAATAAAGCAAC
TGATTGTCCACATGCTTCTGGGAAGCTTGGTGTTCTTGGTTGCAAATATGATACAGATAA
30 CCATCACTCTTGAAGAGAGGTTCTATCAATATGGAGGAAATACAAGTGTAATTCCATGG
AGACTGAGTTCTCAATTTTGATAGAGCTGATGTTATTTAACATGACTATGTTCTCCATTA
TACCATTTTCATTGGCCTTAATTTCTTTTCTTCTGCTAATCTTCTCTTTATGGAAACATC
TCCAGAAGATGCCACTCAATTCTAGAGGAGATAGAGACCCTAGTGCTACGGCCCACAGAA

ATGCCTTGAGAATTTTGGTCTCCTTCCTCTTGCTCTATACTATATATTTCTGTCTCTTC
 TTATATCATGGGTTGCTCAGAAGAATCAAAGTGAAGTGGTTCACATTATTTGTATGATAA
 CTTCACTCGTGTATCCTTCATTCCACTCATATATCCTGATTCTGGGAAATTATAAATTAA
 AGCAGACCTCTCTTTGGGTAATGAGGCAGCTGGGATGTAGGATGAAAAGACAGAATACAC
 5 **CAACTACATAAGGCAGCCAAACAGTCTATTGGGTTTTAGATAACAAATCTAAATCTATGA**
 GGAAGTAGTTCAATAACATTTTTCCCCTTGACATGGAGTAGCAGGGTTTTTTTTTTATTAG
 ATATTTTCTTTACTTACATTTCAAATGCTATCCCGAAAATTCCCTGTACCCTCTCCCTGT
 CCTGTTCCCCTACCCACCCACTCCCCTTCTTGGCCCTGGCATTCCCCTGGAGTATCAGT
 TTTTTATTAGTCAAACATCTCACTGACTAAGGGTCATAAAACAAGTTATTTTAACTA
 10 ATTTCAATTAAATCAAAGGTAAAGTGTGAGCACATGCCTTTAATCACACAATTCCATCAA
 ATTCAGCACTCAGGAGAGGGTGATCTCTGTGAATTCCAGCACACTGGCGGCCGTTACTAG
 TGGATCCGAGCTCGGTACCAAGCTT

15 **SEQ ID NO:153**

Mouse T2R25 amino acid sequence

MMGIAIDILWAAIIIVQFIIGNIANGFIALVNIIDWVKRRKISLMDKIIITALAISRIYLL
 WSTFLITLTSSLDPDIKMAVKIIRISNNTWIIANHFISIWFATCLSIFYFLKIANFSNYIF
 20 LYLRWRFKKVSVTLLISLIFLLLNILLNMHIDIWSDKSKRNLSFSVRSNNCTQFPRLV
 LLINTMFTSIPFTVSLLAFLLLIFSLWRHLKTMQYYAKGSEDTTAAHIKALHMOVAFLL
 FYTVFFLSLAIQYWTSGSQENNNLFYATIVITFPSVHSCILILRNSQLRQASLLVLWVLL
 CKSKDVRMLVP

25

SEQ ID NO:154

Mouse T2R25 nucleotide sequence

AAAACTATTTCGAATTGAACACAGTAACCAATTCTTCAGCGGACTTACACAAATCAAGCTA
 30 TTATCTTATGGATGATGGGTATTGCCATAGATATCTTATGGGCAGCTATTATCATTGTGC
AATTCATAATTGGGAATATTGCAAATGGATTCATAGCATTGGTGAACATCATAGACTGGG
TGAAGAGAAGAAAAATCTCTTTAATGGATAAGATCATTACTGCTTTGGCAATCTCTAGGA
TTTATCTGCTGTGGTCTACATTCTTAATTACACTAACATCTTCACTGGATCCAGATATTA
AAATGGCTGTGAAATCATTAGAATAAGCAATAACACCTGGATTATTGCAAATCATTTCA

GCATTTGGTTTGCTACATGTCTCAGCATCTTTTATTTTCTCAAGATAGCCAATTTTCTA
ACTATATTTTCTCTACTTAAGGTGGAGATTTAAGAAGGTGGTTTCAGTGACATTGCTAA
TCTCTCTTATCTTCCTGCTTTTAAATATTTTACTGATGAACATGCATATTGATATCTGGA
GTGATAAGTCCAAAAGAAACCTTTCTTTTAGTGTCAGATCAAATAATTGCACTCAGTTTC
5 CCAGACTTGTCTTTTAATCAACACAATGTTACATCAATCCCCTTCACTGTGTCCCTGT
TGGCTTTTCTGCTTCTCATCTTCTCCCTGTGGAGACACCTGAAAACCATGCAATACTATG
CTAAAGGCTCCGAAGACACCACCACAGCTGCACATATAAAGGCCTTGCACATGGTAGTGG
CCTTTCTCCTGTTCTACACAGTTTTCTTTTTGTCTCTTGCCATACAATATTGGACCTCTG
GGTCTCAAGAGAATAACAACCTGTTTTATGCCACAATTGTAATTACTTTCCCTTCAGTCC
10 ATTCATGTATCCTGATTCTGAGAAACAGCCAGCTGAGGCAGGCATCTCTGTTGGTGCTGT
GGTGGCTGCTGTGCAAGTCCAAAGATGTACGGATGTTGGTTCCCTGAAATACTCTGTCAA
TGCTCTTTAGTAGTGAAGAAGAAAATAGCTTAGTTAAGGAAATTCTTGTTCAATTACCGAA
GTATACTTTCAAGTTTATGTATC

15

SEQ ID NO:155

Mouse T2R26 amino acid sequence

MLPTLSVFFMLTFVLLCFLGILANGFIVLMLSREWLLRGRLLPSPDMILFSLGTSRFFQQC
20 VGLVNSFYFFLHLVEYSGSLARQLISLHWDFLNSATFWFCTWLSVLFCIKIANFSPHAPFL
WLKWRFPALVPWFLLGSILVSVIVTLLFFWGNHTIYQAFLLRRKFTGNTTFKEWNRRLRID
YFMPLKVVTMSIPCSLFLVSILLISSLRHSLRMQHNTSLQDPNVQAHSRALKSLISF
LVLYAVSFVSMIIDATVFISSDNVWYWPWQIILYFCMSVHPFILITNNLRFRTFRQLLL
LARGFWVA

25

SEQ ID NO:156

Mouse T2R26 nucleotide sequence

GAATTCTAGACAAGGAAAGACACACTAAATGACTTTACTTGTGGGACCTAAAATAACC
30 AAAATAAGTCAAAATCACAGTGATGTTACTAGGGATCTAGGATAAGGGAATGAAGAGAAA
GATGTTGGTCATAGAGTACAAAAATTCAGCTAAGAACTCAGTCCTGGAGGCTGAATGTAT
AGCTGTGTGACAGACAGCAGCTAGCCATACCAGAGTATACACTTGCCTCTTGCTGAAAGA
GTAGATCTTATGTGTCCTTGTACACATAAAAGTAATTGAAAAAGTAACTCTCTGAGATG

ACAGATACGTTAAATGGTTTTACTTTTCAACCTGCTCCAGTAGGGGTCCCTTTAATGTT
 TGTGCTAGTAGATGGGGGACTCTCAAGTATCTTTGTGGTAGACAAATCTAAGGTGGCCTT
 CATGAATACCAACCCAGACTTTTGTGACTTTGTGATCCCCACTTTTGAAGTGGATAAGA
 GCTGTGACTTGAGTCTAATCAAAGGAGTCCAACGTGTTGTTTATTCTGTAACAGTGCTTT
 5 GTGTTTCTAGTTAATAACACAGGCAAAGAAGGCTAGGGTGACATTCCTAGGATTGTGTTA
 TTTCTATCTTGCTCATGCCTCCCTCTGCTGGTCTAATGAAATAAGTCAGTGGCCATATTT
 AAATATGACTACGTGGCAAATACTGATGATAGCCTGTGTGTTCCAACAAATATCCAGTAG
 GAGACCTAGGCATTGAGTCTGCAGCCACAAGGAAATAGGTTCTTTCACTGGAAAAAGAG
 CAGTTTAGATGGTTATAAATTACTTAATCCATAGAAGCCATAGGGGCTTTATGTAGAGAT
 10 TTGGGTAGAGAGGTAGACCTAGATATTGACTTAGGAGTGGCTATTCCTGAGTGGGGGTAG
 ATATATGGCAGGGGAACTCAGATAAGAAAGACTTCTTTAGTGTACGATTTTTCTAGGT
 ATCTCCTTGTGCCAGATATCTATGCGTCTATGTACCTACCTACCTACCTACCTACCTACC
 TACCTACCTACCTACTGACACCTAATAGGAAGAGGCAAGTGGTCACAACCTGCAATGATG
 GGATAAGAATGATGGAACCTCAGTTACCAAGATTAAAATACCTTCCCCACTGATGTTATTG
 15 CAAGCATGGCAGCATGTAGGCAAATCAGAGAAGGCAAATCATGAGCAGCTGCTGCCCCA
 TGGTACCCGAGCCCGGAAATATTTGCATCATATCTGAGCCAAAAGCACACCTTTTATCT
 ACTGCCTGAGCATTTTTTACATTGAAGTTCTGGCTCACATGCAGAATCCAACCATTATC
 TCCTGTCTCCAGAAGGGAGTGTGAGGGACTGTGGGTAGGGGCAGGGAGGAGGCCAGGAAC
 CAAGGCAATCAGTGGTGACAGGAGGAGGGACTGAAATGCTACCAACATTATCAGTTTTCT
 20 TCATGTTGACCTTTGTTCTGCTCTGTTTCCTGGGGATCCTGGCCAACGGCTTCATTGTGC
 TGATGCTGAGCAGGGAATGGCTACTGCGTGGTAGGCTGCTCCCCTCGGACATGATCCTCT
 TCAGTTTGGGCACCTCCCGATTCTTCCAGCAGTGTGTGGGATTGGTCAACAGTTTCTATT
 ACTTCCTCCATCTGGTTGAGTACTCCGGGAGCCTTGCCCGGCAGCTCATTAGTCTTCACT
 GGGACTTCTTGAACTCAGCCACTTTCTGGTTTTGTACCTGGCTCAGCGTCCTGTTCTGTA
 25 TCAAGATTGCTAACTTCTCCATCCTGCCTTCCTGTGGTTGAAGTGGAGATTCCCAGCGT
 TGGTGCCCTGGTTCTTGTGGGCTCTATCTTGGTGTCCGTCATTGTAACCTCTGCTGTTCT
 TTTGGGGAAACCACACTATATATCAGGCATTCTTAAGGAGAAAGTTTACTGGGAACACAA
 CCTTTAAGGAGTGGAAACAGAAGGCTGGAAATAGACTATTTTCATGCCTCTGAAAGTTGTCA
 CCATGTCAATTCCTTGTTCTCTTTTTCTGGTCTCAATTTTGCTGTTGATCAGTTCTCTCA
 30 GAAGGCATTGCTAAGAATGCAGCACAATACCCACAGCTTGCAAGACCCCAACGTCCAGG
 CTCACAGCAGAGCCCTGAAGTCACTCATCTCATTCCTGGTTCTTTATGCGGTGTCCTTG
 TGTCATGATCATTGATGCTACAGTCTTCATCTCCTCAGATAATGTGTGGTATTGGCCCT
 GGCAAATTATACTTTACTTTTGCATGTCTGTACATCCATTTATCCTCATCACCATAATC
 TCAGGTTCCGCGGCACCTTCAGGCAGCTACTCCTGTTGGCCAGGGGATTCTGGGTGGCCT

AGAAGGCTTGGTCTCTTTATCTAGAGCCTTTGAAGAGACTCAGGTGAGGGTAACTTCACT
TGGAAGTGAGCTCATCTACGTGGAAATGTCTTTGTAGGCAGGCATGGGGTCATACTGTGA
GGTTCCTCATTGGGAAAGAGGAGAAGAAAATACAGAGTGTCTTCCTTACCTTAGGATAT
TATGAAAGTGGAATTCCGAATCCTGGACCAGTATTGATCTAAGTGCAAAGTACAATATG
5 **TCCTGTTTCCTTTCATGTCTGTTTTTCCTTTTGTACTGATTCATTCTCTAGGGAATAGTCT**
TGATCAACTGAATCATCTCATCTGGCTGGCCACTGGGGAGGTAAAAGAACTTTGTGTCAC
TGCTGCATTGGGATATACATGGGTGGGAAGCAAGTGTCCCTGAGGCAGAGTAGCACTCAG
TATGAGAACCTCAAAGAGCAGGTGGCTGTGCATGCAGGGGCTGGGGCAAGGAGTCCTGAT
CACTCTTCACTGTATGGGGATTATTTGTCTCTTGCCAAAATTTGGAGACTTTGGCTTTAG
10 **TTTTGTGAAGATGACTGGAAAAATTCTTAATGCTACCCTGTATCATTTCTCAATAATATT**
TTCTTTTTCCTGCCTTTAATTTTCTCCTATCTGCAGCGCCCCTTGCTTGTTATCCGTAAA
TAAATAAATAAATAAATAAATAAGCCCAATCCTCATTTTCCTGTCTTTGGGAACCCTTTT
ACTTCCCCAGGTATACGCTACAAAGCCACTTCTGCATTGAATAAACATTATCTTTCATTC
AGAAAAAGACTTAAGAATCTCACCTTTACAAAAAAAAAAAAAAAAAAGAATCTCACTTATTT
15 **TATATTCAAATTCCATTTTTTAAAAAGAAAAGCACAGCATTAAATTTTTCTAAATACTGTTT**
ATAAAAAATAACTTGCTCTAAGAATTATACAAATGTTTTGAAAGGTAACTTTGGAAAAAAA
GTGTGATTAGACATGGATGTTTGTAAGACAGAACAAAGAGCTCTTGGAAGTCCATGGCAG
CTCATTGGTCTTGCCCTCAGTAGAGCCTGTCTGAATCCTGTAACCTCTTATGCCCTTTTG
TAGCTTTTCTGCAGATC

20

SEQ ID NO:157

Mouse T2R27 nucleotide sequence

25 **GAATTCGCCCTTGCGGGATCCGGGAACGGATTCATAGCACTGGTAAACTTCATGGGCTGG**
ATGAAGAATAGGAAGATTGCCTCCATTGATTTAATCCTCACAAGTCTGGCCATATCCAGA
ATTTGTCTATTGTGCGTAATACTATTAGATTGTTTTATATTGGTGCTATATCCAGATGTC
TATGCCACTGGTAAAGAAATGAGAATCATTGACTTCTTCTGGACACTAACCAATCACTTA
AGTATCTGGTTTGCAACCTGCCTCAGCATTTACTATTTCTTCAAGATAGGTAATTTCTTT
30 **CACCCACTTTTCCTATGCCTCAAGTCTAGACGCCAAGGGC**

SEQ ID NO:158

Mouse T2R28 amino acid sequence

GREWLR YGRLLPLDMILISLGASRFCLQLVGTVHNFFYSSAQKVEYSGGLGRQFFHLHWHF
LNSATFWFCSWLSVLCVKIAN

5

SEQ ID NO:159

Mouse T2R28 nucleotide sequence

GAATTCGCCCTTGCGGGATCCGGGAACGGGTTTATTGTGCTGGTGCTGGGCAGGGAGTGG
10 CTGCGATATGGCAGGTTGCTGCCCTTGGATATGATCCTCATTAGCTTGGGTGCCTCCCGC
TTCTGCCTGCAGTTGGTTGGGACGGTGCACAACTTCTACTACTCTGCCCAGAAGGTCGAG
TACTCTGGGGGTCTCGGCCGACAGTTCTTCCATCTACACTGGCACTTCTGAACTCAGCC
ACCTTCTGGTTTTGCAGCTGGCTCAGTGTCTGTTCTGTGTGAAGATTGCTAACATCACA
CACTCCACCTTCTGTGTCTCAAGTCTAGACGCCAAGGGCG

15

SEQ ID NO:160

Mouse T2R29 amino acid sequence

MDGIVQNMFTFIVIVEIIIGWIGNGFIALVNCIHWHYKRRKISALNQILTALAFSRIYLLL
TVFTVIAVSTLYTHVLVTRRVVKLINFHLLFSNHFSMWLAACLGLYYFLKIAHFPNSIFV
YLKMRINQVVSGTLLMSLGLLFLNLTLLINSYIDTKIDDYREHLLYDFTSNNTASFYRVIL
VINNCIFTSIPFTLSQSTFLLLIIFSLWRHYKKMQQHAQRCRDVLADAHIRVLQTMVTYVL
LCAIFFLSLSMQILRSELLKNILYVRFCEIVA AVFPSGHSCVLICRDTNLRGTFLSVLSW
25 LKQRFTSWIPNINCRSSCIF

SEQ ID NO:161

Mouse T2R29 nucleotide sequence

30

AGCTTGATATTTCTATTTGTTACTGCACAGAGTTTTTTTTTAAAAATTGAGTTTGTTATG
TGGATTCAATACTCAGATAGAGCTCTTTAATTTTTTTACAGTGACCTCATGAATCATAAC
TTGCCTTACAGACAATGGATGGAATCGTACAGAACATGTTTACATTCATTGTAATTGTGG
AAATAATAATAGGATGGATTGGAAATGGATTTCATAGCTCTGGTGAAGTGCATACACTGGT

ACAAGAGAAGAAAGATCTCTGCACTGAATCAAATACTCACAGCCTTGGCTTTCTCCAGAA
TCTACCTTCTTTTAACAGTATTCAC TGTATAGCAGTGTCTACGCTATACACACACGTGT
TGGTAACTAGAAGAGTGGTAAACTGATTAATTTCCATTTGCTTTTCAGCAATCATTTTA
GCATGTGGCTTGCTGCATGCCTTGGCCTTTATTATTTTCTTAAAATAGCTCATTTTCCTA
5 ACTCTATTTTTGTTTACTTAAAGATGAGAATTAACCAGGTGGTTTCAGGGACTTTGCTCA
TGTCTTTGGGCCTCTTGTCTTAAACACTCTGCTGATAAACTCATACATTGATACCAAGA
TAGATGACTACAGAGAACATCTACTGTATGATTTCACTTCGAATAATACTGCTTCATTTT
ACAGGGTTATTTTAGTCATTAACAAC TGTATTTTCACATCTATACCCTTTACACTTTCCC
AGTCCACTTTTCTCCTGCTCATCTTCTCCCTGTGGAGACATTACAAGAAGATGCAACAGC
10 ATGCACAAAGATGCAGAGATGTCCTTGCAGATGCCACATCAGAGTCTTGCAAACCATGG
TCACCTATGTCCTACTCTGTGCCATTTTCTTTCTGTCTCTTTCCATGCAAATTTTGAGGA
GTGAGTTGTTGAAGAACATTCTTTACGTTAGGTTCTGCGAGATTGTTGCAGCAGTTTTTC
CTTCAGGACACTCCTGTGTCTTAATCTGTAGAGACACAAACCTGAGAGGGACCTTTCTTT
CTGTGCTATCGTGGCTGAAGCAGAGGTTTACATCATGGATTCCTAACATAAATTGCAGAT
15 CATCTTGCATATTCTAAAGAAACTGAG

SEQ ID NO:162

Mouse T2R30 amino acid sequence

20 MTYETDTTLMMLVAVGEALVGILGNAFIALVNFMGWMKNRKIASIDLILSSVAMSRICLQC
IILLDCIILVQYPDTYNRGKEMRTVDFFWTLTNHLSVWFATCLSIFYLFKIANFFHPLFL
WIKWRIDKLILRTL LACV IISLCFSLPVTENLSDDFRRVCVKTKERINSTLRCKV NKAGHA
SVKVN LNLVMLFPFSVSLVSFLLLILSLWRHTRQIQLSVTGYKDPSTTAHV KAMKAVISF
25 LALFVVYCLAFLIATSSYFMPES ELAVIWGELIALIYPSSH SFILILGSSKLKQASVRVL
CRVKTMLKGKKY

SEQ ID NO:163

30 Mouse T2R30 nucleotide sequence

AAAAATGTTTCATTGTTTATCTAAAATTCAAATTTAACTGAGTGCCCTACATTTTTATTTA
TTCAATCTAGTAGCTGTACTGAGGTTATTAGTGTGATTTCTGAAGCCCAAATTTGTAAAA
CTTAGCCTCAGATAAACAGCTTGAGACCATGGAAAGTAATTTGGTAAATTTGCATCTTAG

CAAATAGTAGCTCAGCCTAAATTAACCTGTGTGTAGAAAAGAATGACCTGCGGAGAAGATA
 AATGGACATACAATATCCAGGCTAAGGATTGCCAAACACACTGTTTTTAAGACTAATTGA
 GATTTAGATAAACTATCTACAGTCTTCATGTATAATTCTCATCTTCATCACAAGACAGAC
 TTCAACTTAAGGAGGTAAAGACAAGGACAGCGAACCCCTAAACAGCCAAGTGTAGAAACCA
 5 AACTGCATCAAATCAGCCAGAACTAATTGGATACTTCTCTACTTTAAAATGACATACGA
 AACAGATACTACCTTAATGCTTGTAGCTGTTGGTGAGGCCTTAGTAGGGATTTTAGGAAA
 TGCATTCAATTGCACTGGTAAACTTCATGGGCTGGATGAAGAATAGGAAGATTGCCTCTAT
 TGATTTAATCCTCTCAAGTGTGGCCATGTCCAGAATTTGTCTACAGTGTATAATCCTATT
 AGATTGTATTATATTGGTGCAGTATCCAGACACCTACAACAGAGGTAAAGAAATGAGGAC
 10 CGTTGACTTCTTCTGGACACTTACCAACCATTAAAGTGTCTGGTTTGCCACCTGCCTCAG
 CATTTTCTATTTATTCAAGATAGCAAACCTTCTTCCACCCTCTTTTCTCTGGATAAAGTG
 GAGAATTGACAAGCTAATTCTCAGAACTCTACTGGCATGTGTGATTATCTCCCTGTGTTT
 TAGCCTCCCAGTCACTGAAAATCTGAGTGATGATTTTCAGACGTTGTGTTAAGACAAAGGA
 GAGAATAAACTCTACTTTGAGATGCAAAGTAAATAAAGCTGGACATGCCTCTGTCAAGGT
 15 AAATCTCAACTTGGTCATGCTGTTCCCCTTTTCTGTGTCTCTGGTCTCCTTTCTCCTCTT
 GATCCTCTCCCTGTGGAGACACACCAGGCAGATACAACCTCAGTGTAACAGGGTACAAAGA
 TCCCAGCACAAACAGCTCATGTGAAAGCCATGAAAGCAGTAATTTCTTCTGGCCCTGTT
 TGTGTCTACTGCCTAGCCTTTCTCATAGCCACCTCCAGCTACTTTATGCCAGAGAGTGA
 ATTAGCTGTAATATGGGGTGAGCTGATAGCTCTAATCTATCCTTCAAGCCATTCATTTAT
 20 CCTCATCCTGGGGAGTAGTAACTAAACAAGCATCTGTGAGGGTGCTTTGTAGAGTAAA
 GACCATGTTAAAGGGAAAAAATATTAGCATCATGAGCATATCTGAAGAAAACTATCAC
 TTTCTAAGAGAAAGGAAGACACGATCATTATCCGTCCTTTTCACATGAATATTGATTTCA
 TGCAGTGACATCCTCTTAACAACTTAAATTGAACCTTGAGAAATCTCATATACAGCAAC
 TTTGCATGTCTCTATCTCTGCTTTTTCTCTCCTTTTCAATATGAGTTGACATAAAAAATA
 25 ATTTTCAGAACAAATTATAACAGAAGAAAGGGCATTTCATAATCAGTTCTGAATCACTC
 CTCCAAATGCAAAGCTGCCTGACAAATTCAAACAATTGTAACAGCATCTCACTGTCGTT
 TGCATTCTTTGGAAAAGCAGGTGGTTTGTCTTGGAGCCTGGCTTAGAGTTTTCTTCTTA
 GACCATTGAATTATGTTTCATGATTGGAGAAGAGTCAAGTACCAAGTAACAATTTTTATTG
 TGAAGATGGGTGTTTCATCATGTGATTTTGGCTGGCCTGGAACCTTGTTATGTAGACTAGTC
 30 TGTCATCAAACACACAAAGATCTGCCTGCCTCACCTGCCAGTTCTAGGATTCAAGGAATG
 CACCACCACAGCTTGTTCAAGTGACAATTCTTACAAATGTTTTAGAAATAAATAATATAC
 TAGAAATTAACACTGAATGTAAGTGCTGTTTAGGTATAAATTATGATTAAATGTTATAGT
 TAGAAAATTATTTAAGATTATAGATCAGTGATGAAAATATTCTAGAATAAGTTTTATGAA
 GAACTTTTATAAAGAACTGGAAAAAATCTCTTGATTGCATATTGAAACAAATTTCTC

CAAAAGAACACCTACAAATTTGCTCTAGACATCTAGACTGTATCAAACAGTGAATATGA
 AAATATCATAACAGGATATAGCCTTTAGTATTGAAGACAGGTTCATCTATATTAAACCTG
 CATAACATACTAAAGACTAAGTCAATATCCCACAAACATATTTGCACTATCATGTCTAT
 TGAAACACTATTCATAGTAGCTAAAATATGGCACAAACTAGACATTCATCAATAGATGA
 5 ATCAATAAAGCAAATGTACATACACAAGATGAAATTGTATTCAGGCATAAAGAAGAATGC
 AGTCATGTCATTAGCAAAAACATAAACAGAATTGGAGGTCATTGTGATAATTGAAATAAA
 CCAGACCTGGAAAAACAAAACCTGTGTAATTTTTCTGAAGTAGAGAATATACTCTTGGA
 TGGATAGATGGGTACTGTTATAGTATAAAATGTGTGTGTGTGTGTGTGTGTGTGTGTGTG
 TATTTTCATGAAAGCAAGAATGGGACTGCTTAGAGAAAAGAAAAGGACAAACAGGTGAAGGG
 10 GTGAAAGAAAAGGCAATGACAAGGAGTAATGATATGAGCAAAGTACCATTATTAAACAT
 GTGACAATATTATATAGAAACACATGATTTTGTGTGCCTACCAAACTGGATAATAATTT
 TTAAAATGTATCTATTAAAAGGAAAGAAAAGAAAGTGCAAGCCCAGGAAAGGGAGAAAAG
 GAAACAATGAGAGAGAAATGGAAAATGGTGAGAAGTGAAGAGAACAAAAAGAAATGGAGT
 AAGTGTGGCCAGGAATGAAGGATCTCAGCTATAGTTATCCCAGTACGGTAATACAAATCT
 15 GTGACTCCAGCACTTGACAAGGCTGAGAGATGTGAGAGAGGGCCAGTTAACAACCAGTCT
 GGGCTTATTCCAAGAGATAAGAAGATTGGGGGAAAGTATGTAGAAGGGTTTGGAGGGGAAG
 AGAGAGAAGAGGGAAATGATGTAATGATAGTACAAATCAAAGTTATTTTTTCTAAAAAA
 GCAATGGGACAGGAAACCAACCTAACAAGTAAAGGTGCTTGGTTTACAAGACCAGCAACC
 TGAGTGCATCCTTGCTAGAAATGAAATTGGCCTTACTCTGGAAAGCTTACTTCCTCAGTGT
 20 ATTCATTGTTAAAATTCATGTGGAGATTTTAAAGAAAAAAGGAAAAAAAAGTTAAATGG
 TAGATTTGTGTAGGGGAATATTCCCCTAATTAATTGATTAGATAATAAAGATGACAAGCA
 AATTGCTGTGCAAAAAGGAAGACAAGGTCTAAGAGGGGAAGAGGGGACACGGGAGGAAAA
 AAAACGGCCCTTTTTTAAAGCAAGGTGGGGAGTGAGGGAAGCGAGATGTAGACAGGGAACT
 GTTAGACCTGGTGGCAGCTTCTGCCACCTGAAGATTTTCAACATAGTATAGTTCATGAGT
 25 TTAGGAAGATATGTTCCCTGCCAGCGGTTGTATCATCTGTTGATTTTAACTAAGATTG
 TCTGGTGTTTTCCATTTGCGGAGACTCAAGTAGACCAAAGGGAAAGAATGAATTC

SEQ ID NO:164

30 Mouse T2R31 amino acid sequence

MYMILVRAVFITGMLGNMFIGLANCSDWVKNQKITFINFIMVCLAASRISSVLMLFIDAT
 IQELAPHFYYSYRLVKCSDIFWVITDQLSTWLATCLSI FYLFKVAHISHPLFLWLKWRLR
 GVLVVFVLVFSLFLLISYFLLLETLPWGDYVTLKNNLT LFSGTIKTTAFQKIIVFDIY

LVPFLVSLASLLLLFLSLVKHSRSLDLISTTSEDSRTKIHKKAMKMLVSFLILFIIHIF
MQLARWLLFLFPMSPINFILTLNIFALTHSFILILGNSNLRQRAMRILQHLKSQLOELI
LSLHRFSSLY

5

SEQ ID NO:165

Mouse T2R31 nucleotide sequence

CTGCAGCTTTCTAGAAATCTCACCAGAATGTCTTTGTGCAGCTTTAATAGTTCCTGGTTA
10 TACCTTGTACATTATAAGCTAAGACATCTTTGGTGCCACAATATACTCTCACTAATCAG
AGAGATTAGACAGAAAAATAAGTTTCTTAACAACGTGTTTATAGATAGGGTCATGAAATGAC
ATAAAACACCAATGCTAAGGCAATCCATTATGTTTTCTCATGAGGAGCCCATATGTACAC
TTGAGTGTGTCTTATTATTTCCCTGAGTGATTTTGTAAATTTTATTAAACACTTAACTGTG
ATTCATACTAGTTAGTTCTGAAATTCCTTTCTTCATCAAAGCCATTAATCCTGGGGTTTT
15 TTAAATGGAGAACCCCAAACAAAGTGAAATGTTGTGTGTGGAGCAGGCTGTCTTCCCAC
ACACTACCATGAGATGCTCATTCTGTAATTGTTCCCCGGAATAGGAAATGCCCTGAATTC
AGGCACACAAGAGCTAGTCTGTGCACCATGTCTGGTTCTTGCATTAATACCCACTTTTGT
CACGAAGCTTCATTGATTCGCATCTTCAGAAGCTGGTATCATTATTAGTTTCTTTCCTCA
GGTGACTCTGGnCCAAAATATTAnGGCGCCCTTTAAAAAAGTAAACTACAAAATTTCTT
20 TATAATTTTCTTTAAGTTTGTTATAATATAGCATGACCTACACACACACACACACACA
CACACACACACACACACAAGTATGCCTCTCCTTTCTTCTAATAATCTCACTTAAAGC
AATTGTTTAGCTGTCTTCGAAGTCTAGACTGCCACTGTCGTGCTTCTAGCCAAAACAAAT
GCAACACATAAAATGATAGAGCTCAAACTTAGGAATCTATTTAACTGTGAAGATCACGC
AAGCAAACCTGAGAAACCTCTAGAAGGAAACCACAGCAAATCACTGGAGAGAAGGTGTTA
25 ATCTAGTAAGAATAGTTTTTATTTTGGGTATCCTTTTGTAGATTGGTTAGTTCATCCAAA
ATCCAACCTGTTAGTTCTTCATAAATTGTAAGTGTCTCCAACATCAAAGCACCCTTCTC
TCTTTTCCCCTGTATGAAGATGCTTTAAGTACAGAGTTACTCTTTTTCTGTACTGACAGT
AATTTAAAAAAATTTGTTCACTCATTCCTTTTTTGGTGTTGTTATTCTGTGTTCTCAATGT
TATCTTTTTTTTTTCAAACCTTCTTTTATAAAAAGTCATACACATAGCAAATGCAGTGC
30 ATGTTTATGGAATCCATAACTAATTATTGAGACTTCTCCTAGTACTTTCTTTGAACAGT
AACAAAGATATCTGCTTCTACAGAGTGCAGTGTTCAGGTGAGGAGGAACATATTATACA
AATCAGTGAAAAAAAATCTGATTCAAATTTGTATTTTAAATATATTTGACTTTATCACTT
CAGATATTACATCAATGGGAATTTTGAAGGCACACAAGTGATGATGTGGGCATAGAGACT
GTCTGTACTAGAATTTAATATTTCTTTTAAATATCTTTAAATAAAAATATGATGCTGTAT

TCATAAACAGATCTTTATAGATTAAAGTATGAGATTAAAGTTGGAAAAACAAAAGACAAAA
ACCTAGGACTAAGAATTTCCCTTAAGTATGTGTGAATATCAACCTAATGGAGGAAGTTTCC
AATCAAAGCTGAAATTACAGTAAAAAGGAGGAAGATAAATATGGAAAAGGATGATTTTCT
GTGGAAGTTTGTGTGAGAACTGATCCACGAGACAAATTGCTAG**AAG**TGTGGATTCCCTTT
5 TACTATTCAACTGCTTATAGGACTGGATCAA**ATGTATATGATACTGGTAAGAGCAGTATT**
TATAACTGGAATGCTGGGAAATATGTTCAATTGGACTGGCAAACTGCTCTGACTGGGTCAA
GAACCAGAAAATCACCTTCATCAACTTCATCATGGTCTGTTTGGCAGCTTCAGAATCAG
CTCTGTGCTGATGTTATTTATTGATGCAACCATAACAAGAACTAGCGCCTCATTTCTATTA
TTCTTACCGTCTAGTAAAATGCTCTGATATATTCTGGGTATAACTGATCAACTATCAAC
10 **ATGGCTTGCCACCTGCCTGAGCATATTCTACTTATTCAAAGTAGCCACATTTCCCATCC**
CCTTTTCCTCTGGTTGAAGTGGAGATTGAGAGGTGTGCTTGTTGTTTTCTTGATTTTTC
TTTGTTCTTATTGATTTCTTATTTTCTACTGCTTGAAACACTTCCTATTTGGGGAGATAT
TTATGTAACCCTTAAAAACAATCTGACCTTATTTTCAGGTACAATTAAGACCACTGCTTT
TCAAAAGATAATTGTTTTTGATATAATATATTTAGTCCCATTTCTTGTTGTCCCTAGCATC
15 **ATTGCTCCTTTTATTTTTGTCTTGGTGAAACACTCCCGAAGCCTTGACCTGATTTCTAC**
CACTTCTGAAGATTCCAGAACCAAGATTCATAAGAAGGCCATGAAAATGCTGGTGTCTTT
CCTCATTCTCTTTATAATTCACATTTTTTTTCATGCAGTTAGCACGGTGGTTATTATTTTT
GTTTCCAATGAGCAGGCCAATTAATTTTCATCTTAACATTAAATATCTTTGCCTTAACTCA
CTCATTTATTCTCATCCTGGGAAATAGCAATCTTCGACAGAGAGCAATGAGGATCCTGCA
20 **ACATCTTAAAGCCAGCTTCAAGAGCTGATCCTCTCCCTTCATAGATTCTCCAGTCTTTA**
CTAGAGGAACAGCTTAACAGGGAGACTTGGAAGGTCACTGGCAAATTATTCTTCTTTGAT
TTCTTTTAAGTACTGCTGAACATATATGAACTGTCCCAGAGCATAGTGCTATCTTATGA
GAAGGATATCATCTCACAGTCTGGTTATAAAACACAAACCAATCTTTTTATAATTTCTTT
ACAGCATTGCTAATAAAAGACTTGTAGTCTCAAATATTTTAAAGAGAATAATTAATTTTA
25 TAGGCAAAGGTATGAAATTACAATTCACAGGGAAGGTTCA TGACTCCTTAGATATTA
GTTAATTGTAAGCCACAATAGGCAGAAGATGAGCAAATGTTGATAGGAGATAAATAAAA
TCTAAAGTTACGGAGAAAAAAAACATCAACTTGCCTTTTAGATTACTTTAAAGCTCTCTC
TCTCGCTCTCTCTCTGTATCTACTTACTTTATATATACAAATGTTTTGTCTGCATGTA
TTTCTTTGCACCATATAAATGTCTAAGTATCCAGAA**n**GT**C**AGCAGAGGGCATCAAATTCT
30 CTGGAAAGAGAGTTACAAATTGCTGTGGGTAACACTGGGTGCTGGGAACTAACCTGAGTC
CTCTGCCACAGCAACTGCTCTTCCCTGCTGAGTCATGTTTTAAGTCTCCACA**A**CTTAAAC
TCATTGTTGATGTGGTCATTGCATAATGATGAATTTACATTCTAAGGTTTGTATCATAGG
TAGGAGGGCTGGTTTTAATCATATTCTAATGTTCTTATACAAACCCAGGTTTTGTAAGAG
ACTGTATTCTATCATGAGACTCTTTCCCCACACCGCCAATGTAACATTTTTTATTAATTTT

GAGGGGAATTTTATACAGTGTACCCTGATCACCCCTTGCTTCCCACTCCTTGCAGGTCTAC
 CCTCCCACCATTTGCTCAATCCCCCCTAAAAGAGAGAGAAACAAACCATGTCCAATTTGTG
 TTGGACACATACTCAGTGGAACATGGCCAAACCCCTAGTGAGCAGTTCCCTTAAAGAAAAC
 TAAGCTGCCTCCCCACCACTACCACCATAGGGCATTAACTGTGAAGAGCTACACTTTAGC
 5 TATTTTATCACCAATTTAAAAGACTGTCTTCAATAGCTTCCTCTATGGACTGTTTCTGGT
 TTTAGTGGGACAGGGAGAAGGGGTCAAGAGGTTGTACAGAACTTTTGATGTCTCTTAT
 TCTCAGTTAAAGTCCACTGCAAAGAAGTCTGCTGGCTCTAATAAAGCTTGCAACAGCAT
 GGGCCAGTGACATCATCATGATTTCTGGCAACAATATGGACCACAAATATCATGGCTCAG
 GTGGCATTACGGACCACAGACATCAACATGGTCTCTGGCAGCAAGAACCAGAATCTTTTG
 10 AGGAGGCTTCATTCAGAAAATGAATTTTTCTTCATCCCAGATATACTGATGTTGCTCAAT
 CAGAGTATTAGTATGGTTGGGCACCATATTTGGGGACAGGACCTTCAATATTTCCAGGCT
 GCTGTGTAACACATTATCTTTAGTGTGAGGTGCCCTTAGTGTGAGGACATGACCATCATG
 TATGCGCCTGTGGGCAGAAATACATCTTTGTACTTTCTTACACCTAGCAGGGTGAGTAGC
 AGGAGCAGCGGCATTAATACTTCCATACCTCTGGGCAGCCTATCAGGTATCATCTAGGCA
 15 AGGTAAGCCCAGTAGTGGCCCAAGGCTCCTGGTGTCTACTTGGCAACAACATGCTCCTTT
 GTCTGCACTGCCATATCTATGGCTGGTTCTCCATCCCTAGTTCTGCTTCTCTCAGGTTTT
 ATACGACTCTATTCCACATTCTATTTTTCCAGTTCCATGAAACCAGTGTTTAAAAGTATC
 ATCCCATAAGACCGGCCTTTTAAAGGTTATTCTGGAGATATTGCAGAGTCTGCAG

20

SEQ ID NO:166

T2R Family Consensus Sequence 1

E (F/A) (I/V/L) (V/L) G (I/V) (L/V) GN (G/T) FI (V/A) LVNC (I/M) DW

25

SEQ ID NO:167

T2R Family Consensus Sequence 2

30 (D/G) (F/L) (I/L) L (T/I) (G/A/S) LAISRI (C/G/F) L

SEQ ID NO:168

T2R Family Consensus Sequence 3

NH(L/F) (S/T/N) (L/I/V)W(F/L) (A/T)T(C/S/N)L(S/N/G) (I/V)

5 **SEQ ID NO:169**

T2R Family Consensus Sequence 4

FY(F/C) LKIA(N/S) FS(H/N) (P/S) (L/I/V) FL(W/Y) LK

10

SEQ ID NO:170

T2R Family Consensus Sequence 5

LLI(I/F/V) SLW(K/R) H(S/T) (K/R) (Q/K) (M/I) (Q/K)

15

SEQ ID NO:171

T2R Family Consensus Sequence 6

20 HS(F/L) (I/V) LI(L/M) (G/S/T)N(P/S/N) KL(K/R) (Q/R)